Rapid synthesis of bis(hetero)aryls by one-pot Masuda borylation – Suzuki coupling sequence and its application to concise total syntheses of meridianins A and G **

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Supporting Information

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1. General Considerations

All cross coupling reactions were carried out in oven-dried Schlenk glassware using septa and syringes under nitrogen or argon atmosphere. THF and 1,4-dioxane were dried using *MBraun* system MB-SPS-800, and triethylamine was refluxed under argon atmosphere over ketyl sodium, distilled and stored in a Schlenk flask over potassium hydroxide pellets under argon atmosphere. Dry methanol was purchased from *Sigma-Aldrich Chemie GmbH*.

4,4,5,5-Tetramethyl-1,3,2-dioxaborolane (pinacolborane) was purchased from *Sigma-Aldrich Chemie GmbH* and used as supplied. Tetrakis(triphenylphosphane)-palladium(0) and cesium carbonate were purchased from *Merck Serono KGaA*.

Commercial grade reagents were used as supplied without further purification and were purchased from *Acros Organics*, *Sigma-Aldrich Chemie GmbH*, *Fluka AG*, *ABCR GmBH & Co. KG, Alfa Aesar GmbH & Co. KG*, *Aces Pharma Inc., Interchim Inc., Synthonix Inc., Synchem OHG* and *Merck Serono KGaA*.

Compounds **1h**-**1i**, **1k**-**1n** and **3a**-**3q** are commercially available (see ***Table 1***). Compounds **1a**-**1c**,[1] **1d**-**1g**[2] and **1j**[3] were prepared according to the literature procedures.

The purification of products was performed on silica gel 60 (0.015-0.040 mm) from *Merck Serono KGaA* Darmstadt using flash technique and under pressure of 2 bar. The crude mixtures were adsorbed on Celite® 545 (0.02-0.10 mm) from *Merck Serono KGaA* Darmstadt before chromatographic purification.

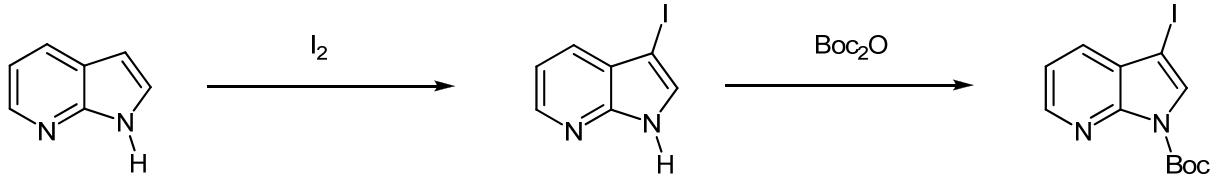
The reaction progress was monitored qualitatively using TLC Silica gel 60 F_{254} 5 x 7.5 cm aluminium sheets obtained by *Merck Serono KGaA* Darmstadt. The spots were detected with UV light at 254 nm and using aqueous potassium permanganate solution.

^{1}H, ^{13}C, and 135-DEPT NMR spectra were recorded on Bruker DRX 500 spectrometer. Acetone-d_6, $CDCl_3$ and DMSO-d_6 were used as deuterated solvents. TMS was used as reference (δ = 0.0) or the resonances of the solvents were locked as internal standards (acetone-d_6: ^{1}H δ 2.05, ^{13}C δ 30.8; $CDCl_3$: ^{1}H δ 7.26, ^{13}C δ 77.0; DMSO-d_6: ^{1}H δ 2.50, ^{13}C δ 39.4). The multiplicities of signals were abbreviated as follows: s: singlet; d: doublet; t: triplet; dd: doublet of doublets, ddd: doublet of doublets of doublets, dt: doublet of triplets, td: triplet of doublets, tt: triplet of triplets, q: quartet, quint: quintet, sext: sextet, m: multiplet and br: broad signal. The type of carbon atoms was determined on the basis of 135-DEPT NMR spectra.

EI mass spectra were measured on Finnigan MAT 8200 spectrometer. IR spectra were obtained on Bruker Vector 22 FT-IR. The solids were measured as KBr pellets and oils as films on KBr plates. The intensity of signals is abbreviated as follows: s (strong), m (medium) and w (weak). The melting points (uncorrected) were measured on Reichert-Jung Thermovar. Combustion analyses were carried out on Perkin Elmer Series II Analyser 2400 in the microanalytical laboratory of Institut für Pharmazeutische und Medizinische Chemie der Heinrich-Heine-Universität Düsseldorf.

2. Preparation of Starting Materials 1a, 1c, 1f and 1j

2.1. Preparation of tert-butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (1a)[1]



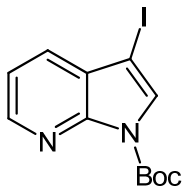
1a

A solution of iodine (25.7 g, 101 mmol) in 180 mL DMF was dropped to the solution of 7-azaindole (12.1 g, 100 mmol) and potassium hydroxide (16.5 g, 250 mmol) in 180 mL DMF at room temperature and the mixture was stirred for 45 min. The reaction mixture was then poored on 1 L ice water containing 1 % ammonia and 0.2 % sodium disulfite. The precipitate was filtered, washed with ice water and dried in vacuo to obtain 23.7 g (97.2 mmol, 97 % yield) of a yellow solid.

The obtained solid was used without further purification for the next step. It was suspended in 180 mL dichloromethane, 4-dimethylaminopyridine (1.21 g, 9.72 mmol) was added and di-*tert*-butyl dicarbonate (32.8 g, 146 mmol), dissolved in 180 mL dichloromethane, was added dropwise for 30 min. The mixture was stirred for 30 min. at room temperature, washed with 200 mL 0.1 *N* HCl, and the aqueous phase was extracted with dichloromethane (2 x 100 mL). The combined organic layers were dried with sodium sulphate, the solvents were removed under reduced pressure and the residue was adsorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 5:1, R_f (PE-EtOAc = 20:1): 0.14) to give 31.6 g (91.8 mmol, 94 % yield; 92 % total yield over two steps) of **1a** as an orange oil, which solidifies upon storage in refrigerator.

[1] B. Witulski, N. Buschmann, U. Bergsträßer, *Tetrahedron* **2000**, *56*, 8473-8480.

tert-Butyl 3-iodo-1_H_-pyrrolo[2,3-_b_]pyridine-1-carboxylate (1a)



$C_{12}H_{13}IN_2O_2$

344.15

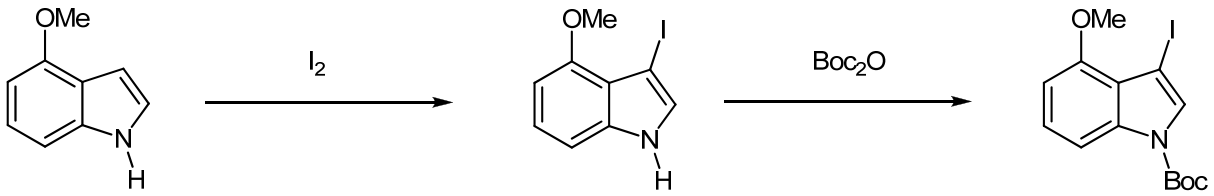
31.6 g (91.8 mmol, 92 % yield over two steps) as a yellow oil (solidified upon storage in refrigerator). Mp 79 °C. ^{1}H NMR (acetone-d_6, 300 MHz): δ 1.67 (s, 9 H), 7.36 (dd, J = 8.1 Hz, J = 4.8 Hz, 1 H), 7.75 (dd, J = 8.1 Hz, J = 1.5 Hz, 1 H), 7.99 (s, 1 H), 8.44 (dd, J = 4.8 Hz, J = 1.5 Hz, 1 H). ^{13}C NMR (acetone-d_6, 75 MHz): δ 28.1 (CH_3), 61.9 (C_{quat}), 84.8 (C_{quat}), 120.1 (CH), 125.8 (C_{quat}), 130.1 (CH), 132.1 (CH), 146.6 (CH), 147.8 (C_{quat}), 147.9 (C_{quat}). EI + MS (*m/z* (%)): 344 (M^+, 7), 271 ($(M-C_4H_9O)^+$, 3), 245 (10), 244 ($(M-C_5H_9O_2+H)^+$, 100), 217 ($(M-I)^+$, 5), 162 ($C_8H_6N_2O_2^+$, 13), 144 ($C_8H_4N_2O^+$, 1), 127 (I^+, 2), 117 ($C_7H_5N_2^+$, 14), 116 ($C_7H_4N_2^+$, 8), 57 ($C_4H_9^+$, 22).

Data reported in the literature:

T. A. Kelly, D. W. McNeil, J. M. Rose, E. David, C.-K. Shih, P. M. Grob, *J. Med. Chem*. **1997**, *40*, 2430-2433.

^{1}H NMR ($CDCl_3$): δ 1.70 (s, 9 H), 7.28 (dd, J = 8.5 Hz, 1 H), 7.72 (dd, J = 8.1 Hz, 1 H), 7.80 (s, 1 H), 8.49 (dd, J = 5.1 Hz, 1 H).

2.2. Preparation of tert-butyl 3-iodo-4-methoxy-1H-indole-1-carboxylate (1c)[1]



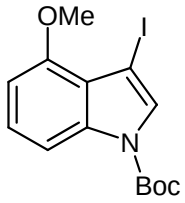
1c

A solution of iodine (2.57 g, 10.1 mmol) in 15 mL DMF was dropped to the solution of 4-methoxy-1*H*-indole (1.50 g, 10.0 mmol) and potassium hydroxide (1.65 g, 25.0 mmol) in 15 mL DMF at room temperature and the mixture was stirred for 45 min. The reaction mixture was then poored on 200 mL ice water containing 1 % ammonia and 0.2 % sodium disulfite. The precipitate was filtered, washed with ice water and dried in vacuo to obtain 3.34 g (8.58 mmol, 86 % yield) of a gray solid.

The obtained solid was used without further purification for the next step. It was suspended in 15 mL dichloromethane, 4-dimethylaminopyridine (106 mg, 0.86 mmol) was added and di-*tert*-butyl dicarbonate (2.90 g, 12.9 mmol), dissolved in 15 mL dichloromethane, was added dropwise for 25 min. The mixture was stirred for 30 min at room temperature, washed with 15 mL 0.1 *N* HCl, and the aqueous phase was extracted with dichloromethane (4 x 15 mL, monitored by TLC). The combined organic layers were dried with sodium sulphate, the solvents were removed under reduced pressure and the residue was adsorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 100:1 → 50:1 (stepwise gradient), R_f (PE-EtOAc = 50:1): 0.21) to give 3.08 g (8.24 mmol, 96 % yield; 82 % total yield over two steps) of **1c** as a pale yellow oil, which solidifies upon storage in refrigerator to a pale yellow amorphous solid.

[1] B. Witulski, N. Buschmann, U. Bergsträßer, *Tetrahedron* **2000**, *56*, 8473-8480.

tert-Butyl 3-iodo-4-methoxy-1_H_-indole-1-carboxylate (1c)

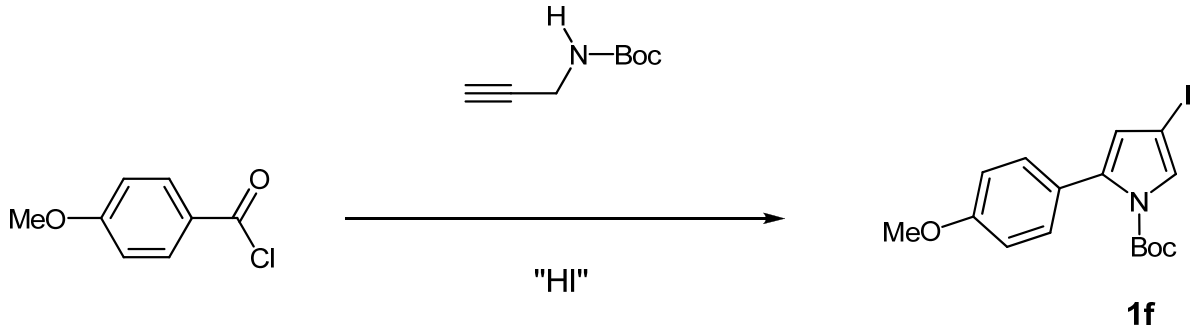


$C_{14}H_{16}INO_3$

373.19

3.08 g (8.24 mmol, 82 % yield over two steps) as a pale yellow oil (solidified upon storage in refrigerator). Mp 68 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.64 (s, 9 H), 3.92 (s, 3 H), 6.67 (d, *J* = 8.2 Hz, 1 H), 7.24 (t, *J* = 8.2 Hz, 1 H), 7.61 (s, 1 H), 7.80 (d, *J* = 8.2 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 28.1 (CH_3), 55.4 (CH_3), 57.6 (C_{quat}), 84.2 (C_{quat}), 104.0 (CH), 108.0 (CH), 119.6 (C_{quat}), 125.9 (CH), 130.0 (CH), 136.5 (C_{quat}), 148.5 (C_{quat}), 153.2 (C_{quat}). EI + MS (*m/z* (%)): 373 (M^+, 33), 317 ($(M-C_4H_9+H)^+$, 100), 273 ($(M-C_4H_9+H-CO_2)^+$, 56), 258 ($(M-C_4H_9+H-CO_2-CH_3)^+$, 23), 57 ($C_4H_9^+$, 83). IR (film): $\tilde{\nu}$ 3151 (w) cm^{-1}, 2979 (s), 2937 (m), 2837 (w), 1732 (s), 1606 (m), 1586 (s), 1494 (s), 1427 (s), 1394 (m), 1370 (s), 1339 (s), 1286 (s), 1153 (s), 1124 (s), 1046 (s), 955 (w), 903 (w), 852 (m), 819 (w), 775 (m), 735 (m), 696 (w), 668 (w), 597 (w). Anal. calcd for $C_{14}H_{16}INO_3$ (373.2): C 45.06, H 4.32, N 3.75. Found: C 45.07, H 4.11, N 3.56.

2.3. Preparation of tert-butyl 4-iodo-2-(4-methoxyphenyl)-1H-pyrrole-1-carboxylate (1f)[2]

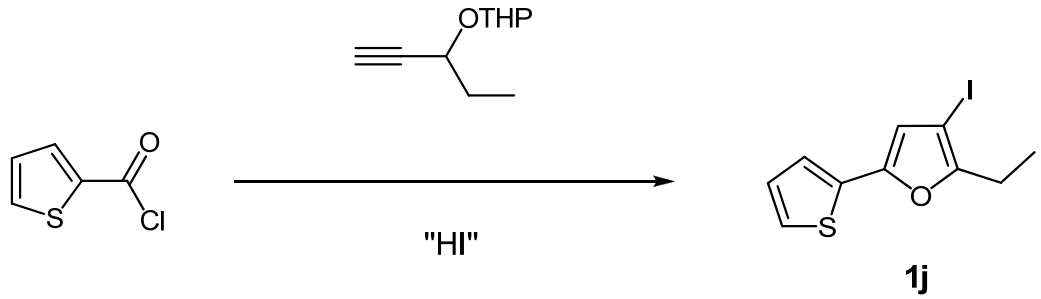


1f

$PdCl_2(PPh_3)_2$ (425 mg, 0.60 mmol, 2 mol %) and CuI (233 mg, 1.20 mmol, 4 mol %) were placed under argon atmosphere in a screw-cap vessel, which was then dried with a heat gun and cooled to room temperature (water bath). Then, 150 mL of dry THF were added and the mixture was degassed with argon. Dry triethylamine (4.16 mL, 30.0 mmol), 4-methoxybenzoyl chloride (5.28 g, 30.0 mmol), and *tert*-butyl prop-2-ynylcarbamate (4.66 g, 30.0 mmol) were successively added to the mixture which was stirred at room temperature for 1 h (monitored by TLC). Then, sodium iodide (22.7 g, 150 mmol), toluene-4-sulfonic acid monohydrate (11.6 g, 60.0 mmol) and 30 ml of *tert*-butanol were successively added to the mixture which was stirred at room temperature for 1 h (monitored by TLC). The reaction mixture was diluted with 300 mL brine, the phases were separated and the aqueous phase was extracted with dichloromethane (3 x 150 mL). The combined organic layers were dried with anhydrous sodium sulfate. After removal of the solvents in vacuo the residue was absorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 100:1) to give 9.23 g (23.1 mmol, 77 % yield) of the desired product (**1f**) as a colorless solid.

[2] “Three-component synthesis of *N*-Boc-4-iodopyrroles and sequential one-pot alkynylation“ E. Merkul, C. Boersch, W. Frank, T. J. J. Müller, *Org. Lett.* **2009**, *11*, 2269-2272.

2.4. Preparation of 2-ethyl-3-iodo-5-(thiophen-2-yl)furan (1j)[3]

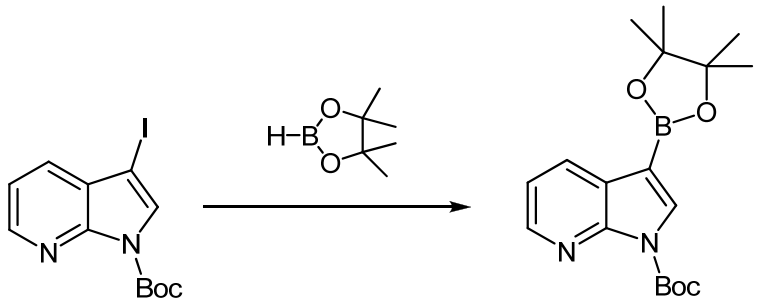


$PdCl_2(PPh_3)_2$ (142 mg, 0.20 mmol, 2 mol %) and CuI (78 mg, 0.40 mmol, 4 mol %) were placed under argon atmosphere in a screw-cap vessel, which was then dried with a heat gun and cooled to room temperature (water bath). Then, 50 mL of dry THF were added and the mixture was degassed with argon. Dry triethylamine (1.39 mL, 10.0 mmol), thiophene-2-carbonyl chloride (1.50 g, 10.0 mmol), and tetrahydro-2-(pent-1-yn-3-yloxy)-2*H*-pyran (4.66 g, 10.0 mmol) were successively added to the mixture which was stirred at room temperature for 2 h (monitored by TLC). Then, sodium iodide (7.57 g, 50.0 mmol), toluene-4-sulfonic acid monohydrate (2.14 g, 11.0 mmol) and 30 ml of methanol were successively added to the mixture which was stirred at room temperature for 2 h (monitored by TLC). After removal of the solvents in vacuo the residue was absorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 10:1) to give 2.72 g (8.93 mmol, 89 % yield) of **1j** as an orange oil.

“A novel one-pot three-component synthesis of 3-halofurans and sequential Suzuki coupling“ A. S. Karpov, E. Merkul, T. Oeser, T. J. J. Müller, *Chem. Commun.* **2005**, 2581-2583.

[3] “One-pot three-component synthesis of 3-halofurans and 3-chloro-4-iodofurans” A. S. Karpov, E. Merkul, T. Oeser, T. J. J. Müller, *Eur. J. Org. Chem.* **2006**, 2991-3000.

3. Preparation of *tert*-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate (2a)

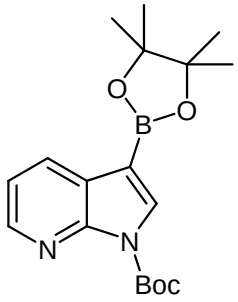


1a **2a**

Tetrakis(triphenylphosphane)-palladium(0) (35 mg, 0.03 mmol, 3 mol %) and *tert*-butyl 3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate (**1a**) (344 mg, 1.00 mmol) were placed under argon atmosphere in a dry screw-cap vessel with septum. Then, 5 mL of dry dioxane were added and the mixture was degassed with argon. Dry triethylamine (1.39 mL, 10.0 mmol, 10.0 equiv), and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.22 mL, 1.50 mmol, 1.50 equiv) were successively added to the mixture which was stirred at 80 °C (preheated oil bath) for 3 h (monitored by TLC). Then, after cooling to room temperature (water bath), the solvent was removed in vacuo and the residue was absorbed onto Celite® and purified chromatographically* on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 5:1) to give 291 mg (0.85 mmol, 85 % yield) of **2a** as a yellow solid. Recrystallization from *n*-pentane gave colorless crystals.

*The purification was performed on Biotage SP-1 system using a 50 g silica gel SNAP cartridge.

tert-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1_H_-pyrrolo[2,3-_b_]pyridine-1-carboxylate (2a)



$C_{18}H_{25}BN_2O_4$

344.21

291 mg (0.85 mmol, 85 % yield) as a yellow solid. R_f (PE-EtOAc = 5:1): 0.30. Mp 97-98 °C. ^{1}H NMR (acetone-d_6, 500 MHz): δ 1.37 (s, 12 H), 1.68 (s, 9 H), 7.28 (dd, J = 7.6 Hz, J = 4.7 Hz, 1 H), 8.05 (s, 1 H), 8.21 (dd, J = 7.9 Hz, J = 1.9 Hz, 1 H), 8.40 (dd, J = 4.7 Hz, J = 1.6 Hz, 1 H). ^{13}C NMR (acetone-d_6, 125 MHz): δ 26.2 (CH_3), 29.2 (CH_3), 85.3 (C_{quat}), 85.6 (C_{quat}), 120.7 (CH), 127.7 (C_{quat}), 132.2 (CH), 137.6 (CH), 146.5 (CH), 149.5 (C_{quat}), 150.8 (C_{quat}), 207.1 (C_{quat}). EI + MS (*m/z* (%)): 344 (M^+, 10), 244 (100), 229 (28), 185 (10), 171 (9), 158 (37), 144 (62), 118 (12), 57 (13). Anal. calcd for $C_{18}H_{25}BN_2O_4$ (344.2): C 62.81, H 7.32, N 8.14. Found: C 62.75, H 7.39, N 8.10.

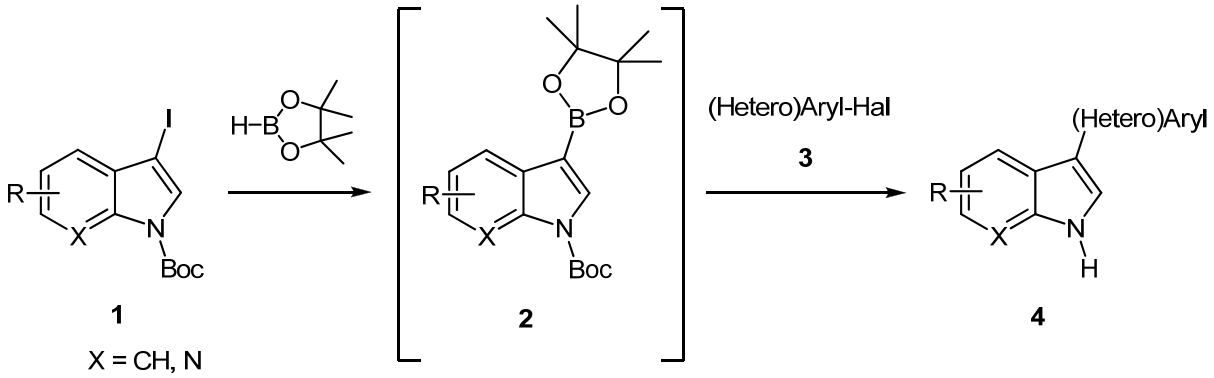
Data reported in the literature:

V. A. Kallepalli, F. Shi, S. Paul, E. N. Onyeozili, R. E. Maleczka Jr., M. R. Smith III, *J. Org. Chem.* **2009**, *74*, 9199-9201.

White solid. Mp 115-117 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.33 (br s, 12 H), 1.62 (br s, 9 H), 7.16-7.18 (dd, J = 7.8 Hz, J = 4.6 Hz, 1 H), 8.01 (br s, 1 H), 8.20-8.22 (dd, J = 7.8 Hz, J = 1.7 Hz, 1 H), 8.45-8.46 (dd, J = 4.9 Hz, J = 1.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 24.8 (CH_3), 28.1 (CH_3), 83.5 (C_{quat}), 84.3 (C_{quat}), 118.8 (CH), 126.1 (C_{quat}), 130.9 (CH), 135.4 (CH), 145.1 (CH), 147.6 (C_{quat}), 149.3 (C_{quat}), 207.1 (C_{quat}). GCMS (EI) (*m/z* (%)): 244 (100), 229 (38), 187 (35), 158 (37), 144 (46), 117 (11). ^{11}B NMR ($CDCl_3$, 96 MHz): δ 30.2. Anal. calcd for $C_{18}H_{25}BN_2O_4$ (344.2): C 62.81, H 7.32, N 8.14. Found: C 63.18, H 7.59, N 8.09.

4. Preparation of Compounds 4a-u by the *Masuda* Borylation – *Suzuki* Coupling Sequence

4.1. General Procedure



Tetrakis(triphenylphosphane)-palladium(0) (35 mg, 0.03 mmol, 3 mol %) and *tert*-butyl 3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate (**1a**) (344 mg, 1.00 mmol) were placed under argon atmosphere in a dry screw-cap vessel with septum. Then, 5 mL of dry dioxane were added and the mixture was degassed with argon. Dry triethylamine (1.39 mL, 10.0 mmol, 10.0 equiv), and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.22 mL, 1.50 mmol, 1.50 equiv)* were successively added to the mixture which was stirred at 80 °C (preheated oil bath) for 3 h (monitored by TLC). Then, after cooling to room temperature (water bath), 5 mL of dry methanol, 1.00 mmol of (hetero)aryl halide **3** and cesium carbonate (823 mg, 2.50 mmol, 2.50 equiv) were successively added and the mixture was stirred at 100 °C overnight (preheated oil bath; for exact reaction times, see ***Table 2***). Then, after cooling to room temperature (water bath) the solvents were removed in vacuo and the residue was absorbed onto Celite® and purified chromatographically on silica gel with dichloromethane-methanol-aqueous ammonia (isocratic or stepwise gradient). The obtained bis(hetero)aryls **4** can be further purified by suspending in dichloromethane, sonication in ultrasound bath for 0.5-1.0 h, filtration and drying in vacuo overnight.

*For the preparation of compounds **4r**-**4t**, 3.00 equiv (0.44 mL, 3.00 mmol) of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (pinacolborane) were used.

The experimental details are given in ***Table 1***.

Table 1. Experimental details for the synthesis of bis(hetero)aryls **4**.

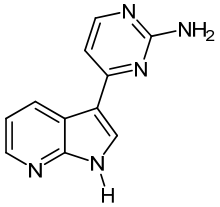
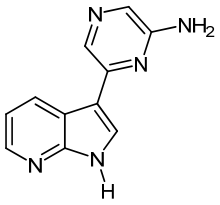
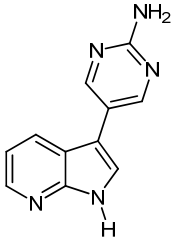
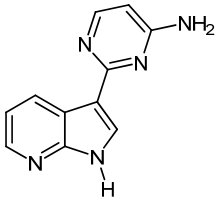
Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) UV purity
1	*tert*-Butyl 3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate 344 mg (1.00 mmol) **1a**	4-Chloro-pyrimidin-2-amine (*Synchem*) 134 mg (1.00 mmol) **3a**	Pale yellow solid 134 mg (0.63 mmol, 63 %)  **4a**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 HT-LC-MS: 100 %
2	344 mg (1.00 mmol) **1a**	6-Chloro-pyrazin-2-amine *(Synthonix)* 132 mg (1.00 mmol) **3b**	Green-brown solid 112 mg (0.53 mmol, 53 %)  **4b**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 → 100:7:1 HT-LC-MS: 100 %
3	344 mg (1.00 mmol) **1a**	5-Iodo-pyrimidin-2-amine (*Alfa Aesar*) 228 mg (1.00 mmol) **3c**	Pale yellow solid 139 mg (0.66 mmol, 66 %)  **4c**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 HT-LC-MS: 100 %
4	344 mg (1.00 mmol) **1a**	2-Chloro-pyrimidin-4-amine (*Aldrich*) 134 mg (1.00 mmol) **3d**	Beige solid 79 mg (0.37 mmol, 37 %)  **4d**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 HT-LC-MS: 98.1 %

Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls **4**.

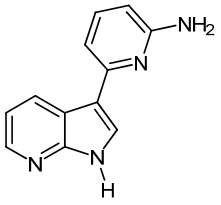
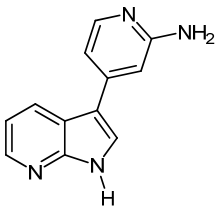
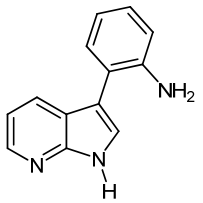
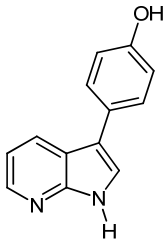
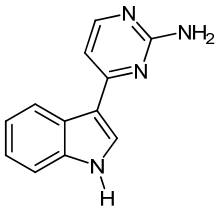
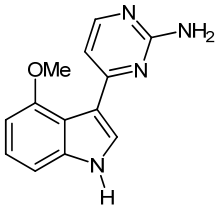
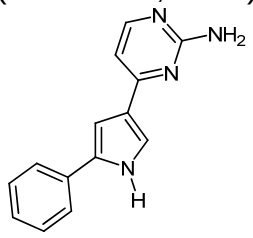
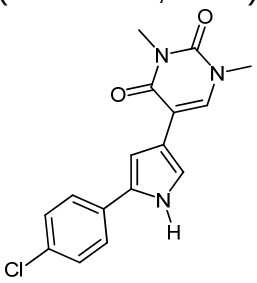
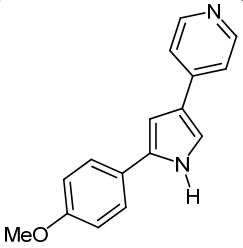
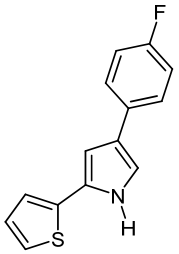
Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) UV purity
5	*tert*-Butyl 3-iodo-1*H*-pyrrolo[2,3-*b*]pyridine-1-carboxylate 344 mg (1.00 mmol) **1a**	6-Bromo-pyridin-2-amine (*ABCR*) 177 mg (1.00 mmol) **3e**	Pale yellow solid 170 mg (0.81 mmol, 81 %)  **4e**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 HT-LC-MS: 100 %
6	344 mg (1.00 mmol) **1a**	4-Bromo-pyridin-2-amine (*Interchim*) 173 mg (1.00 mmol) **3f**	Yellow solid 135 mg (0.64 mmol, 64 %)  **4f**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 → 100:7:1 HT-LC-MS: 100 %
7	344 mg (1.00 mmol) **1a**	2-Iodo-benzen-amine (*Merck*) 221 mg (1.00 mmol) **3g**	Pale yellow solid 154 mg (0.74 mmol, 74 %)  **4g**	DCM-MeOH-NH_3 = 100:1:1 HT-LC-MS: 100 %
8	344 mg (1.00 mmol) **1a**	4-Iodo-phenol (*Alfa Aesar*) 222 mg (1.00 mmol) **3h**	Beige solid 120 mg (0.57 mmol, 57 %)  **4h**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 HT-LC-MS: 97.5 %

Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls **4**.

Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) UV purity
9	*tert*-Butyl 3-iodo-1*H*-indole-1-carboxylate 343 mg (1.00 mmol) **1b**	4-Chloro-pyrimidin-2-amine (*Synchem*) 134 mg (1.00 mmol) **3a**	Pale yellow solid 154 mg (0.73 mmol, 73 %)  **4i**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 HT-LC-MS: 99.6 %
10	*tert*-Butyl 3-iodo-4-methoxy-1*H*-indole-1-carboxylate 373 mg (1.00 mmol) **1c**	134 mg (1.00 mmol) **3a**	Colorless solid 185 mg (0.77 mmol, 77 %)  **4j**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 HT-LC-MS: 100 %
11	*tert*-Butyl 4-iodo-2-phenyl-1*H*-pyrrole-1-carboxylate 369 mg (1.00 mmol) **1d**[a]	134 mg (1.00 mmol) **3a**	Rosa solid 190 mg (0.80 mmol, 80 %)  **4k**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 HT-LC-MS: 98.2 %

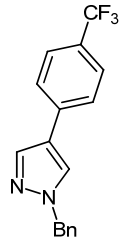
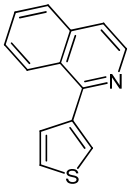
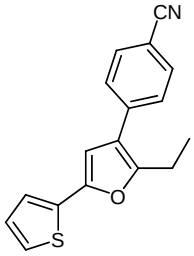
[a] "Three-component synthesis of *N*-Boc-4-iodopyrroles and sequential one-pot alkynylation" E. Merkul, C. Boersch, W. Frank, T. J. J. Müller, *Org. Lett.* **2009**, *11*, 2269-2272.

Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls **4**.

Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) R_f (eluent) UV purity
12	*tert*-Butyl 2-(4-chloro-phenyl)-4-iodo-1*H*-pyrrole-1-carboxylate 404 mg (1.00 mmol) **1e**[a]	5-Iodo-1,3-dimethyl-pyrimidine-2,4(1*H*,3*H*)-dione (5-Iodo-1,3-dimethyl-uracil) (*Aldrich*) 269 mg (1.00 mmol) **3i**	Rosa solid 202 mg (0.64 mmol, 64 %)  **4l**	PE-EtOAc = 2:1 → 1:1 R_f (PE-EtOAc = 1:1): 0.32 HT-LC-MS: 100 %
13	*tert*-Butyl 4-iodo-2-(4-methoxy-phenyl)-1*H*-pyrrole-1-carboxylate 399 mg (1.00 mmol) **1f**[a]	4-Iodo-pyridine (*ABCR*) 214 mg (1.00 mmol) **3j**	Beige solid 151 mg (0.60 mmol, 60 %)  **4m**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 HT-LC-MS: 100 %
14	*tert*-Butyl 4-iodo-2-(thiophen-2-yl)-1*H*-pyrrole-1-carboxylate 375 mg (1.00 mmol) **1g**[a]	1-Fluoro-4-iodobenzene (*ABCR*) 224 mg (1.00 mmol) **3k**	Pale gray solid 170 mg (0.70 mmol, 70 %)  **4n**	PE-EtOAc = 10:1 R_f (PE-EtOAc = 10:1): 0.21 HT-LC-MS: 100 %

[a] "Three-component synthesis of *N*-Boc-4-iodopyrroles and sequential one-pot alkynylation" E. Merkul, C. Boersch, W. Frank, T. J. J. Müller, *Org. Lett.* **2009**, *11*, 2269-2272.

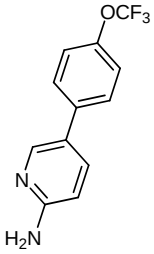
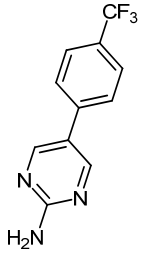
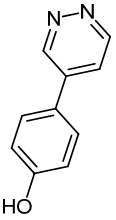
Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls **4**.

Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) R_f (eluent) UV purity
15	1-Benzyl-4-iodo-1*H*-pyrazole (*ABCR*) 284 mg (1.00 mmol) **1h**	1-(Trifluoromethyl)-4-iodobenzene (*Alfa Aesar*) 278 mg (1.00 mmol) **3l**	Colorless solid 106 mg (0.35 mmol, 35 %)  **4o**	PE-EtOAc = 7:1 R_f (PE-EtOAc = 7:1): 0.17 HT-LC-MS: 100 %
16	3-Iodothiophene (*Alfa Aesar*) 219 mg (1.00 mmol) **1i**	1-Iodoisoquinoline (*Aldrich*) 263 mg (1.00 mmol) **3m**	Colorless solid 161 mg (0.76 mmol, 76 %)  **4p**	PE-EtOAc = 5:1 R_f (PE-EtOAc = 5:1): 0.35 HT-LC-MS: 100 %
17	2-Ethyl-3-iodo-5-(thiophen-2-yl)furan[b] 304 mg (1.00 mmol) **1j**	4-Iodobenzonitrile (*ABCR*) 234 mg (1.00 mmol) **3n**	Pale yellow solid 221 mg (0.79 mmol, 79 %)  **4q**	PE-EtOAc = 20:1 R_f (PE-EtOAc = 20:1): 0.36 Crystallization by suspension in *n*-pentane, sonication in ultrasound bath, filtration and drying in vacuo overnight HT-LC-MS: 100 %

[b] "A novel one-pot three-component synthesis of 3-halofurans and sequential Suzuki coupling" A. S. Karpov, E. Merkul, T. Oeser, T. J. J. Müller, *Chem. Commun.* **2005**, 2581-2583.

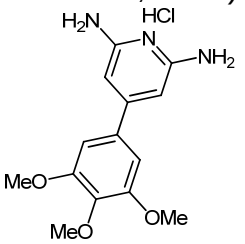
"One-pot three-component synthesis of 3-halofurans and 3-chloro-4-iodofurans" A. S. Karpov, E. Merkul, T. Oeser, T. J. J. Müller, *Eur. J. Org. Chem.* **2006**, 2991-3000.

Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls **4**.

Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) UV purity
18	5-Iodo-pyridin-2-amine (*Alfa Aesar*) 227 mg (1.00 mmol) **1k**	1-Iodo-4-(trifluoro-methoxy)-benzene (*Alfa Aesar*) 294 mg (1.00 mmol) **3o**	Colorless solid 233 mg (0.92 mmol, 92 %)[c]  **4r**	DCM-MeOH-NH_3 = 100:1:1 HT-LC-MS: 100 %
19	5-Iodo-pyrimidin-2-amine (*Alfa Aesar*) 228 mg (1.00 mmol) **1l**	1-(Trifluoro-methyl)-4-iodobenzene (*Alfa Aesar*) 278 mg (1.00 mmol) **3l**	Colorless solid 105 mg (0.44 mmol, 44 %)[c]  **4s**	DCM-MeOH-NH_3 = 100:1:1 HT-LC-MS: 100 %
20	4-Iodophenol (*Alfa Aesar*) 225 mg (1.00 mmol) **1m**	4-Bromopyridazine hydrochloride[d] (*Aces Pharma*) 212 mg (1.00 mmol) **3p**	Rosa solid 121 mg (0.70 mmol, 70 %)[c]  **4t**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 → 100:7:1 HT-LC-MS: 100 %

[c] 3.00 equiv of HBpin have been used in the *Masuda* borylation step.
[d] Since the bromide **3p** was used as a hydrochloride, 3.0 equiv of Cs_2CO_3 were applied in the *Suzuki* coupling step.

Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls **4**.

Entry	Substrate **1**	(Hetero)aryl halide **3**	Bis(hetero)aryl **4** (isolated yield %)	Chromatographic purification (eluent) UV purity
21	5-Iodo-1,2,3-trimethoxy-benzene (*Alfa Aesar*) 300 mg (1.00 mmol) **1n**	4-Bromopyridine-2,6-diamine (*ABCR*) 192 mg (1.00 mmol) **3q**	Orange solid 136 mg (0.44 mmol, 44 %)[e]  **4u**	DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 Purified by dissolving in 1.25 *M* HCl in EtOH (*Fluka*), precipitation with *n*-pentane, filtration and drying in vacuo overnight at 70 °C HT-LC-MS: 98.5 %

[e] The yield was determined after formation of the hydrochloride with solution of HCl in EtOH.

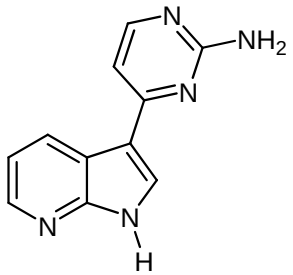
Table 2. Reaction times[a] in the synthesis of bis(hetero)aryls **4**.

Bis(hetero)aryl **4**	*Masuda* borylation step	*Suzuki* coupling step	Bis(hetero)aryl **4**	*Masuda* borylation step	*Suzuki* coupling step
4a	3 h	49 h	**4l**	4 h	23 h
4b	3 h	24 h	**4m**	4 h	19 h
4c	3 h	24 h	**4n**	4 h	19 h
4d	3 h	67 h	**4o**	4 h	18 h
4e	3 h	20 h	**4p**	4 h	17 h
4f	3 h	24 h	**4q**	4 h	23 h
4g	3 h	24 h	**4r**	4 h	17 h
4h	3 h	24 h	**4s**	4 h	18 h
4i	3 h	24 h	**4t**	3 h	19 h
4j	3 h	15 h	**4u**	4 h	18 h
4k	4 h	17 h			

[a] The reaction times for the *Suzuki* coupling step are not optimized. The actual reaction times might be much shorter than indicated. The actual reaction times of the *Masuda* borylation step may also be shorter in some cases.

4.2. Spectroscopic Data of the Compounds 4a-u

4.2.1. 4-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)pyrimidin-2-amine (*Meriolin 1*, 4a)



$C_{11}H_9N_5$

211.22

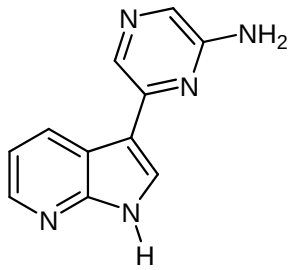
134 mg (0.63 mmol, 63 % yield) as a pale yellow solid. Mp 258-271 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.50 (s, 2 H, N$\underline{H}_2$), 7.06 (d, *J* = 5.4 Hz, 1 H), 7.19 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 8.14 (d, *J* = 5.4 Hz, 1 H), 8.29 (dd, *J* = 4.7 Hz, *J* = 1.6 Hz, 1 H), 8.35 (d, *J* = 2.8 Hz, 1 H), 8.93 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 1 H), 12.2 (br, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 104.9 (CH), 112.4 (C_{quat}), 116.6 (CH), 117.7 (C_{quat}), 128.3 (CH), 130.7 (CH), 143.3 (CH), 149.1 (C_{quat}), 157.2 (CH), 162.0 (C_{quat}), 163.5 (C_{quat}). EI + MS (*m/z* (%)): 212 (16), 211 (M^+, 100), 210 ($(M-H)^+$, 38), 195 ($(M-NH_2)^+$, 2), 170 (14).

Data reported in the literature:

P. M. Fresneda, P. Molina, J. A. Bleda, *Tetrahedron* **2001**, *57*, 2355-2363.

Yellow prisms. Mp 286-289 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 6.47 (s, 2 H, N$\underline{H}_2$), 7.05 (d, *J* = 5.13 Hz, 1 H, H-5´), 7.13 (dd, *J* = 8.12 Hz, *J* = 4.7 Hz, 1 H, H-5), 8.14 (d, *J* = 5.13 Hz, 1 H, H-6´), 8.28 (dd, *J* = 8.12 Hz, *J* = 1.28 Hz, 1 H, H-6), 8.33 (s, 1 H, H-2), 8.92 (dd, *J* = 4.7 Hz, *J* = 1.28 Hz, 1 H, H-4), 12.17 (s, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 105.0 (C-5´), 112.5 (C-3), 116.6 (C-5), 117.8 (C-3a), 128.3 (C-2), 130.6 (C-6), 143.4 (C-4), 143.4 (C-7a), 157.2 (C-6´), 162.0 (C-4´), 163.5 (C-2´). EI + MS (*m/z* (%)): 212 (M^++1, 35), 211 (M^+, 100), 210 (68), 195 (11), 170 (48), 142 (31). IR (nujol): $\tilde{\nu}$ 3473 (m) cm^{-1}, 3294 (m), 3133 (m), 1670 (s), 1565 (s), 1223 (m). Anal. calcd for $C_{11}H_9N_5$ (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.73, H 4.45, N 33.22.

4.2.2. 6-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)pyrazin-2-amine (4b)

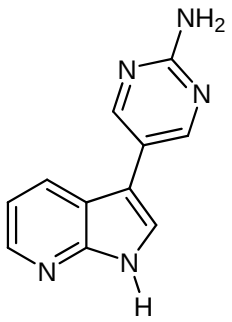


$C_{11}H_9N_5$

211.22

112 mg (0.53 mmol, 53 % yield) as a green-brown solid. Mp 241-243 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.36 (s, 2 H, N<u>H</u>$_2$), 7.17 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 7.67 (s, 1 H), 8.22 (d, *J* = 2.5 Hz, 1 H), 8.27-8.30 (m, 2 H), 8.82 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 1 H), 12.1 (br, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 111.6 (C_{quat}), 116.3 (CH), 117.8 (C_{quat}), 125.8 (CH), 127.6 (CH), 127.9 (CH), 130.1 (CH), 143.2 (CH), 147.7 (C_{quat}), 149.0 (C_{quat}), 155.0 (C_{quat}). EI + MS (*m/z* (%)): 211 (M^+, 100), 184 ($C_{10}H_8N_4^+$, 23), 58 (13), 43 (32), 41 (10). IR (KBr): $\tilde{\nu}$ 3317 (s) cm^{-1}, 3146 (s), 1645 (m), 1575 (w), 1541 (s), 1522 (m), 1495 (m), 1470 (m), 1434 (s), 1366 (w), 1323 (w), 1295 (m), 1280 (w), 1245 (w), 1218 (w), 1139 (w), 1121 (w), 1030 (w), 1001 (w), 886 (w), 825 (w), 796 (w), 772 (w), 697 (w), 633 (w), 586 (w), 528 (w). Anal. calcd for $C_{11}H_9N_5$ (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.47, H 4.38, N 32.92.

4.2.3. 5-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)pyrimidin-2-amine (4c)

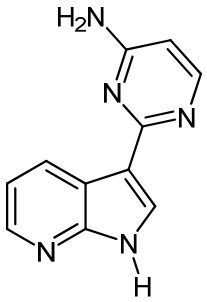


$C_{11}H_9N_5$

211.22

139 mg (0.66 mmol, 66 % yield) as a pale yellow solid. Mp 272 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.61 (s, 2 H, N$\underline{H}_2$), 7.13 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 7.80 (d, *J* = 2.5 Hz, 1 H), 8.20 (dd, *J* = 7.9 Hz, *J* = 1.3 Hz, 1 H), 8.27 (dd, *J* = 4.7 Hz, *J* = 1.6 Hz, 1 H), 8.60 (s, 2 H), 11.9 (br, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 108.9 (C_{quat}), 115.7 (CH), 117.0 (C_{quat}), 117.6 (C_{quat}), 122.3 (CH), 127.3 (CH), 142.8 (CH), 148.7 (C_{quat}), 155.4 (CH), 161.9 (C_{quat}). EI + MS (*m/z* (%)): 211 (M^+, 100), 184 (10), 170 (12), 156 (13), 142 (22). IR (KBr): $\tilde{\nu}$ 3136 (s) cm^{-1}, 1670 (m), 1618 (m), 1534 (s), 1492 (s), 1423 (w), 1335 (w), 1293 (w), 1272 (w), 1219 (w), 1132 (w), 961 (w), 895 (w), 797 (w), 770 (m), 609 (w). Anal. calcd for $C_{11}H_9N_5$ (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.73, H 4.13, N 32.99.

4.2.4. 2-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)pyrimidin-4-amine (4d)

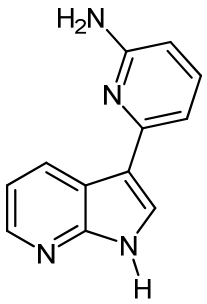


$C_{11}H_9N_5$

211.22

79 mg (0.37 mmol, 37 % yield) as a beige solid. Mp 239 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.23 (d, *J* = 6.0 Hz, 1 H), 6.7 (br, 2 H, N<u>H</u>$_2$), 7.16 (dd, *J* = 7.9 Hz, *J* = 4.4 Hz, 1 H), 8.08-8.11 (m, 2 H), 8.25 (dd, *J* = 4.4 Hz, *J* = 1.6 Hz, 1 H), 8.87 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 1 H), 12.0 (br, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 101.4 (CH), 114.2 (C_{quat}), 116.3 (CH), 118.2 (C_{quat}), 128.0 (CH), 130.4 (CH), 142.9 (CH), 149.0 (C_{quat}), 155.0 (CH), 162.4 (C_{quat}), 163.1 (C_{quat}). EI + MS (*m/z* (%)): 211 (M^+, 100), 210 ($(M-H)^+$, 11), 195 ($(M-NH_2)^+$, 4), 144 (19), 58 (25), 43 (49). IR (KBr): $\tilde{\nu}$ 3418 (m) cm^{-1}, 3316 (m), 3210 (m), 1632 (m), 1579 (s), 1557 (m), 1533 (s), 1467 (s), 1435 (m), 1398 (w), 1369 (m), 1340 (w), 1297 (w), 1238 (w), 1124 (w), 1050 (w), 1019 (w), 984 (w), 901 (w), 828 (m), 803 (w), 777 (w), 671 (w), 599 (w), 530 (w). Anal. calcd for $C_{11}H_9N_5$ (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.48, H 4.37, N 32.99.

4.2.5. 6-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)-pyridin-2-amine (4e)

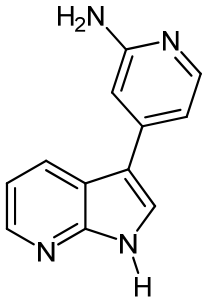


$C_{12}H_{10}N_4$

210.24

170 mg (0.81 mmol, 81 % yield) as a pale yellow solid. Mp 157-158 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.87 (s, 2 H, N<u>H</u>$_2$), 6.26 (dd, *J* = 8.2 Hz, *J* = 0.6 Hz, 1 H), 7.00 (dd, *J* = 7.6 Hz, *J* = 0.6 Hz, 1 H), 7.12 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 7.36 (t, *J* = 7.9 Hz, 1 H), 8.04 (d, *J* = 2.5 Hz, 1 H), 8.24 (dd, *J* = 4.4 Hz, *J* = 1.6 Hz, 1 H), 8.86 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 1 H), 11.9 (br, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 104.2 (CH), 107.3 (CH), 114.6 (C_{quat}), 115.9 (CH), 117.8 (C_{quat}), 125.0 (CH), 130.3 (CH), 137.3 (CH), 142.7 (CH), 149.0 (C_{quat}), 152.8 (C_{quat}), 159.1 (C_{quat}). EI + MS (*m/z* (%)): 210 (M^+, 100), 209 ($(M-H)^+$, 15), 194 ($(M-NH_2)^+$, 5), 183 (26), 182 (15), 155 (16), 39 (11). IR (KBr): $\tilde{\nu}$ 3139 (m) cm^{-1}, 2892 (m), 1633 (m), 1595 (m), 1578 (s), 1528 (s), 1493 (w), 1469 (s), 1454 (s), 1412 (w), 1369 (w), 1339 (w), 1311 (w), 1295 (m), 1273 (w), 1186 (w), 1157 (w), 1129 (w), 895 (w), 819 (w), 800 (s), 771 (m), 733 (w), 675 (w), 630 (w), 582 (w), 525 (w). Anal. calcd for $C_{12}H_{10}N_4$ (210.2): C 68.56, H 4.79, N 26.65. Found: C 68.32, H 4.87, N 26.86.

4.2.6. 4-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)-pyridin-2-amine (4f)

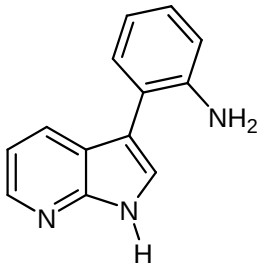


$C_{12}H_{10}N_4$

210.24

135 mg (0.64 mmol, 64 % yield) as a yellow solid. Mp 263-270 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 5.85 (s, 2 H, N$\underline{H}_2$), 6.87 (dd, *J* = 5.4 Hz, *J* = 1.6 Hz, 1 H), 6.89 (s, 1 H), 7.20 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 7.90 (d, *J* = 5.4 Hz, 1 H), 8.00 (d, *J* = 2.5 Hz, 1 H), 8.30 (dd, *J* = 4.7 Hz, *J* = 1.6 Hz, 1 H), 8.33 (dd, *J* = 8.2 Hz, *J* = 1.6 Hz, 1 H), 12.1 (br, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 104.0 (CH), 109.6 (CH), 112.3 (C_{quat}), 116.2 (CH), 117.0 (C_{quat}), 125.2 (CH), 127.6 (CH), 143.0 (C_{quat}), 143.0 (CH), 147.9 (CH), 149.1 (C_{quat}), 160.3 (C_{quat}). EI + MS (*m/z* (%)): 210 (M^+, 100), 210 ($(M-H)^+$, 25), 183 (33), 182 (20), 170 (32), 155 (25), 142 (10), 63 (11), 41 (10), 39 (10). IR (KBr): $\tilde{\nu}$ 3314 (m) cm^{-1}, 3191 (m), 1639 (m), 1607 (s), 1538 (m), 1525 (m), 1507 (w), 1421 (s), 1365 (w), 1323 (w), 1289 (s), 1243 (w), 1174 (w), 1146 (w), 1071 (w), 992 (w), 881 (w), 835 (w), 802 (m), 778 (m), 627 (w), 579 (w). Anal. calcd for $C_{12}H_{10}N_4$ (210.2): C 68.56, H 4.79, N 26.65. Found: C 68.36, H 4.82, N 26.89.

4.2.7. 2-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)-benzenamine (4g)

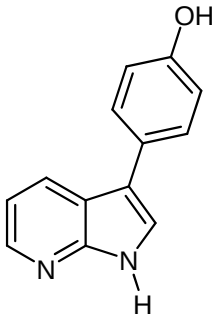


$C_{13}H_{11}N_3$

209.25

154 mg (0.74 mmol, 74 % yield) as a pale yellow solid. Mp 147 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.77 (s, 2 H, N<u>H</u>$_2$), 6.64 (td, *J* = 7.6 Hz, *J* = 1.3 Hz, 1 H), 6.80 (dd, *J* = 8.2 Hz, *J* = 1.3 Hz, 1 H), 7.01-7.05 (m, 1 H), 7.08 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 7.16 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1 H), 7.58 (d, *J* = 2.5 Hz, 1 H), 7.87 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 1 H), 8.26 (dd, *J* = 4.7 Hz, *J* = 1.6 Hz, 1 H), 11.8 (br, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 111.9 (C_{quat}), 115.0 (CH), 115.4 (CH), 116.4 (CH), 118.3 (C_{quat}), 118.8 (C_{quat}), 124.1 (CH), 127.3 (CH), 127.7 (CH), 130.2 (CH), 142.7 (CH), 145.7 (C_{quat}), 148.6 (C_{quat}). EI + MS (*m/z* (%)): 209 (M^+, 100), 208 ($(M-H)^+$, 93), 193 ($C_{13}H_9N_2^+$, 12), 181 (39), 154 (33), 128 (22), 127 (35), 117 ($C_7H_5N_2^+$, 11), 77 (20). IR (KBr): $\tilde{\nu}$ 3364 (m) cm^{-1}, 3142 (s), 3029 (m), 2913 (m), 1614 (s), 1581 (m), 1536 (m), 1490 (m), 1448 (m), 1418 (m), 1339 (w), 1290 (m), 1265 (m), 1152 (w), 1107 (w), 963 (m), 937 (w), 896 (w), 797 (m), 774 (s), 750 (s), 645 (w), 621 (m), 590 (w), 514 (w). Anal. calcd for $C_{13}H_{11}N_3$ (209.3): C 74.62, H 5.30, N 20.08. Found: C 74.43, H 5.14, N 19.95.

4.2.8. 4-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)phenol (4h)

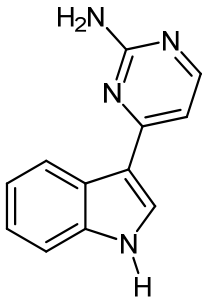


$C_{13}H_{10}N_2O$

210.23

120 mg (0.57 mmol, 57 % yield) as a beige solid. Mp 244 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.85-6.89 (m, 2 H), 7.12 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1 H), 7.50-7.54 (m, 2 H), 7.69 (d, *J* = 2.2 Hz, 1 H), 8.21 (dd, *J* = 8.2 Hz, *J* = 1.3 Hz, 1 H), 8.26 (dd, *J* = 4.7 Hz, *J* = 1.6 Hz, 1 H), 9.39 (s, 1 H, O<u>H</u>), 11.76 (s, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 114.5 (C_{quat}), 115.6 (CH), 115.6 (CH), 117.3 (C_{quat}), 122.2 (CH), 125.8 (C_{quat}), 127.3 (CH), 127.4 (CH), 142.6 (CH), 148.9 (C_{quat}), 155.5 (C_{quat}). EI + MS (*m/z* (%)): 210 (M^+, 100), 209 ($(M-H)^+$, 10), 182 (14), 181 (12), 154 (13), 127 (10), 105 (14), 97 (10), 71 (11), 57 (11). IR (KBr): $\tilde{\nu}$ 3387 (m) cm^{-1}, 3000 (m), 2673 (m), 1604 (m), 1583 (m), 1548 (s), 1504 (m), 1488 (m), 1461 (s), 1438 (s), 1386 (w), 1340 (w), 1324 (m), 1299 (w), 1256 (s), 1169 (m), 1142 (m), 1097 (s), 1043 (w), 964 (m), 836 (s), 817 (m), 797 (m), 774 (m), 578 (m), 540 (m), 503 (w). Anal. calcd for $C_{13}H_{10}N_2O$ (210.2): C 74.27, H 4.79, N 13.33. Found: C 74.04, H 4.86, N 13.62.

4.2.9. 4-(1*H*-Indol-3-yl)-pyrimidin-2-amine (*Meridianin G*, 4i)



$C_{12}H_{10}N_4$

210.23

154 mg (0.73 mmol, 73 % yield) as a pale yellow solid. Mp 195-197 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.42 (s, 2 H, N$\underline{H}_2$), 7.02 (dd, *J* = 5.4 Hz, *J* = 0.6 Hz, 1 H), 7.10-7.15 (m, 1 H), 7.15-7.20 (m, 1 H), 7.43-7.46 (m, 1 H), 8.10 (d, *J* = 5.4 Hz, 1 H), 8.20 (d, *J* = 2.5 Hz, 1 H), 8.59 (d, *J* = 7.9 Hz, 1 H), 11.7 (br, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 105.2 (CH), 111.7 (CH), 113.6 (C_{quat}), 120.1 (CH), 121.8 (CH), 122.3 (CH), 125.2 (C_{quat}), 128.1 (CH), 136.9 (C_{quat}), 156.9 (CH), 162.6 (C_{quat}), 163.4 (C_{quat}). EI + MS (*m/z* (%)): 211 (15), 210 (M^+, 100), 209 ($(M-H)^+$, 34), 169 (60), 141 (10), 140 (14), 105 (12), 97 (12), 85 (10), 83 (10), 71 (12), 57 (14).

Data reported in the literature:

B. Jiang, C.-g. Yang, *Heterocycles* **2000**, *53*, 1489-1498.

Mp 262.2-264.3 °C (EtOAc/MeOH). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 6.39 (br s, 2 H), 7.02 (d, *J* = 5.3 Hz, 1 H), 7.15 (m, 2 H), 7.45 (d, *J* = 7.9 Hz, 1 H), 8.11 (d, *J* = 5.3 Hz, 1 H), 8.19 (s, 1 H), 8.59 (d, *J* = 7.4 Hz, 1 H), 11.65 (br s, 1 H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 105.2, 111.7, 113.6, 120.2, 121.9, 122.3, 125.3, 128.1, 136.9, 156.9, 162.6, 163.4. EI + MS (*m/z* (%)): 210 (M^+, 100), 209 (35), 169 (48), 155 (4), 140 (9), 114 (8), 89 (4). IR (KBr): $\tilde{\nu}$ 3408 cm^{-1}, 3329 , 3174, 1661, 1568, 1453, 1414, 1246, 1119. HRMS calcd for $C_{12}H_{10}N_4$: 210.0923. Found: 210.0914.

M. A. A. Radwan, M. El-Sherbiny, *Bioorg. Med. Chem.* **2007**, *15*, 1206-1211.

Mp 263-265 °C. ^{1}H NMR (DMSO-d_6, 270 MHz): δ 6.4 (br s, 2 H, N<u>H</u>$_2$), 7.03 (d, 1 H, H-5´), 7.15 (m, 2 H, H-5, H-6), 7.44-7.46 (d, 1 H, H-7), 8.11 (d, 1 H, H-6´), 8.19 (s, 1 H, H-2), 8.58-8.61 (d, 1 H, H-4), 11.65 (br s, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 300 MHz): δ 105.2 (C-5´), 111.71 (C-7), 113.70 (C-3), 120.21 (C-3a), 121.85 (C-6), 122.32 (C-5), 125.30 (C-4), 128.10 (C-2), 136.90 (C-7a), 156.91 (C-6´), 162.62 (C-4´), 163.40 (C-2´). EI + MS (*m/z* (%)): 210 (M^+, 100), 209 (36), 169 (49), 155 (4), 140 (10), 114 (8). IR (KBr): $\tilde{\nu}$ 3409 (NH_2) cm^{-1}, 3329 (NH_2), 3172 (NH), 1659, 1569, 1454, 1416, 1241, 1129, 808, 741, 684. Anal. calcd for $C_{12}H_{10}N_4$ (210.2): C 68.56, H 4.79, N 26.65. Found: C 68.72, H 4.76, N 26.47.

G. Simon, H. Couthon-Gourves, J.-P. Haelters, B. Corbel, N. Kervarec, F. Michaud, L. Meijer, *J. Het. Chem.* **2007**, *44*, 793-801.

Yellow powder. Mp 183-185 °C. ^{1}H NMR (acetone-d_6): δ 5.91 (br s, N<u>H</u>$_2$), 7.04 (d, *J* = 5.3 Hz, 1 H, H-5´), 7.10-7.22 (m, 2 H, H-5, H-6), 7.46 (d, *J* = 7.3 Hz, 1 H, H-7), 8.12 (m, 2 H, H-6´, H-2), 8.58 (d, *J* = 7.7 Hz, 1 H, H-4), 10.86 (br s, N<u>H</u>). ^{13}C NMR (acetone-d_6): δ 111.5 (C-5´), 117.2 (C-7), 120.2 (C-3), 126.0/127.7/128.0 (C-4/C-5/C-6), 131.4 (C-3a), 133.0 (C-2), 143.0 (C-7a), 162.7 (C-6´), 168.7/169.5 (C-2´/C-4´). IR (KBr): $\tilde{\nu}$ 3408 cm^{-1}, 3329, 3173, 1660, 1568, 1520, 1452, 1413, 1246, 751, 735. Anal. calcd for $C_{12}H_{10}N_4$ (210.2): C 68.56, H 4.79. Found: C 68.45, H 4.78.

E. Rossignol, A. Youssef, P. Moreau, M. Prudhomme, F. Anizon, *Tetrahedron* **2007**, *63*, 10169-10176.

Beige powder.

F. Tibiletti, M. Simonetti, K. M. Nicholas, G. Palmisano, M. Parravicini, F. Imbesi, S. Tollari, A. Penoni, *Tetrahedron* **2010**, *66*, 1280-1288.

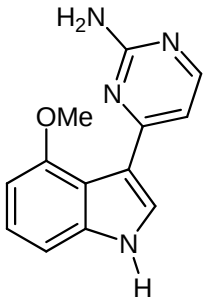
Dark-brown solid. Mp 183 °C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 6.40 (br, 2H), 7.01 (d, *J* = 5.3 Hz, 1 H), 7.18-7.19 (m, 2 H), 7.42 (d, *J* = 7.9 Hz, 1 H), 8.08 (d, *J* = 5.3 Hz, 1 H), 8.18 (d, *J* = 2.9 Hz, 1 H), 8.56 (d, *J* = 7.9 Hz, 1 H), 11.64 (br, 1H). MS (CI): *m/z* 211 (M+1). Anal. calcd for $C_{12}H_{10}N_4$: C 68.56, H 4.79, N 26.65. Found: C 68.47, H 4.81, N 26.72.

L. Núñez-Pons, R. Forestieri, R. M. Nieto, M. Varela, M. Nappo, J. Rodríguez, C. Jiménez, F. Castelluccio, M. Carbone, A. Ramos-Espla, M. Gavagnin, C. Avila, *Polar Biol.* **2010**, *33*, 1319-1329.

^{1}H NMR (DMSO-d_6, 600 MHz): δ 6.38 (s, N$\underline{H}_2$), 7.00 (d, *J* = 5.3 Hz, 1 H, H-5´), 7.10 (t, *J* = 6.8 Hz, 1 H, H-6), 7.16 (t, *J* = 6.8 Hz, 1 H, H-5), 7.42 (d, *J* = 7.9 Hz, 1 H, H-7), 8.08 (d, *J* = 5.3 Hz, 1 H, H-6´), 8.17 (d, *J* = 2.4 Hz, 1 H, H-2), 8.56 (d, *J* = 7.8 Hz, 1 H, H-4), 11.93 (br s, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 300 MHz): δ 105.3 (d, C-5´), 111.8 (d, C-7), 113.2 (s, C-3), 120.2 (d, C-6), 121.9 (d, C-4), 122.4 (d, C-5), 125.2 (s, C-7a), 128.2 (d, C-2), 137.0 (s, C-3a), 157.0 (d, C-6´).

The NMR spectra are in good agreement with those reported in the literature. However, the melting point deviates immensely from the melting point reported by *Jiang* and *Radwan*.

4.2.10. 4-(4-Methoxy-1*H*-indol-3-yl)pyrimidin-2-amine (4j)

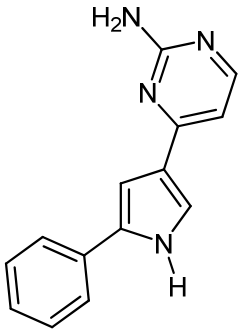


$C_{13}H_{12}N_4O$

240.26

185 mg (0.77 mmol, 77 % yield) as a colorless solid. Mp 221-222 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 3.87 (s, 3 H), 6.27 (s, 2 H, N<u>H</u>$_2$), 6.63 (d, *J* = 6.9 Hz, 1 H), 7.06-7.12 (m, 2 H), 7.26 (dd, *J* = 5.4 Hz, *J* = 0.9 Hz, 1 H), 7.85 (d, *J* = 2.5 Hz, 1 H), 8.15 (d, *J* = 5.4 Hz, 1 H), 11.6 (br, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 55.0 (CH_3), 101.2 (CH), 105.5 (CH), 109.7 (CH), 114.4 (C_{quat}), 115.4 (C_{quat}), 122.7 (CH), 127.5 (CH), 138.8 (C_{quat}), 153.2 (C_{quat}), 157.0 (CH), 161.8 (C_{quat}), 163.2 (C_{quat}). EI + MS (*m/z* (%)): 240 (M^+, 50), 239 ($(M-H)^+$, 21), 211 ($(M-CH_3O+H)^+$, 20), 202 ($(M-C_2H_2N+2H)^+$, 11), 58 ($CH_4N_3^+$, 41), 43 ($C_2H_3O^+$, 100). IR (KBr): $\tilde{\nu}$ 3465 (m) cm^{-1}, 3313 (m), 3165 (m), 1644 (m), 1624 (m), 1575 (s), 1555 (s), 1506 (s), 1459 (s), 1414 (m), 1359 (w), 1320 (m), 1275 (w), 1245 (m), 1212 (w), 1168 (w), 1130 (w), 1088 (m), 970 (w), 884 (w), 815 (w), 778 (w), 733 (m), 706 (w), 630 (w). Anal. calcd for $C_{13}H_{12}N_4O$ (240.3): C 64.99, H 5.03, N 23.32. Found: C 64.86, H 4.85, N 23.25.

4.2.11. 4-(5-Phenyl-1*H*-pyrrol-3-yl)pyrimidin-2-amine (4k)

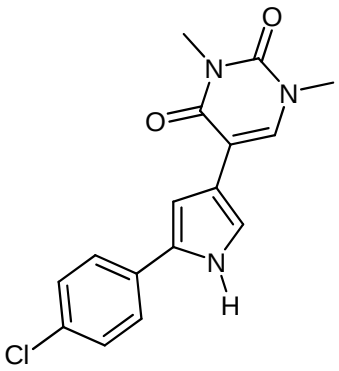


$C_{14}H_{12}N_4$

236.27

190 mg (0.80 mmol, 80 % yield) as a rosa solid. Mp 257 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.35 (s, 2 H, N$\underline{H}_2$), 6.87 (d, *J* = 5.0 Hz, 1 H), 7.06-7.08 (m, 1 H), 7.18-7.23 (m, 1 H), 7.37-7.41 (m, 2 H), 7.58-7.60 (m, 1 H), 7.66-7.70 (m, 2 H), 8.12 (d, *J* = 5.0 Hz, 1 H), 11.7 (br, 1 H, N$\underline{H}$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 104.0 (CH), 104.9 (CH), 120.7 (CH), 123.5 (CH), 123.9 (C_{quat}), 126.0 (CH), 128.7 (CH), 132.1 (C_{quat}), 132.4 (C_{quat}), 157.5 (CH), 161.2 (C_{quat}), 163.5 (C_{quat}). EI + MS (*m/z* (%)): 237 (16), 236 (M^+, 100), 235 ($(M-H)^+$, 22), 195 (35), 133 (13). IR (KBr): $\tilde{\nu}$ 3408 (m) cm^{-1}, 3141 (w), 1631 (m), 1567 (s), 1543 (s), 1509 (w), 1455 (s), 1416 (m), 1369 (w), 1281 (w), 1203 (m), 1156 (w), 1110 (w), 1071 (w), 1031 (w), 990 (w), 926 (w), 900 (w), 874 (w), 815 (m), 793 (w), 751 (s), 694 (m), 593 (w), 528 (w). Anal. calcd for $C_{14}H_{12}N_4$ (236.3): C 71.17, H 5.12, N 23.71. Found: C 71.30, H 5.30, N 23.98.

4.2.12. 5-(5-(4-Chlorophenyl)-1*H*-pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4l)

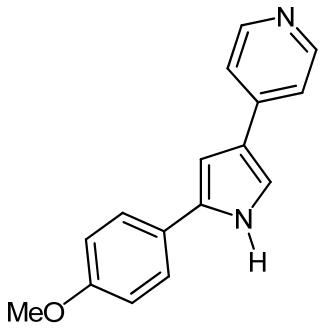


$C_{16}H_{14}ClN_3O_2$

315.75

202 mg (0.64 mmol, 64 % yield) as a rosa solid. Mp 256 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 3.25 (s, 3 H), 3.38 (s, 3 H), 6.93 (dd, *J* = 2.5 Hz, *J* = 1.6 Hz, 1 H), 7.41-7.45 (m, 2 H), 7.49 (dd, *J* = 2.5 Hz, *J* = 1.6 Hz, 1 H), 7.61-7.64 (m, 2 H), 8.04 (s, 1 H), 11.4 (br, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 27.6 (CH_3), 36.3 (CH_3), 103.3 (CH), 107.3 (C_{quat}), 116.7 (C_{quat}), 118.7 (CH), 124.8 (CH), 128.7 (CH), 129.8 (C_{quat}), 131.4 (C_{quat}), 137.8 (CH), 150.5 (C_{quat}), 161.5 (C_{quat}). EI + MS (*m/z* (%)): 317 ((M(^{37}Cl)$^+$, 36), 316 (20), 315 (M(^{35}Cl)$^+$, 100), 258 (22), 229 (11), 217 (27), 203 (13), 201 (28), 189 (18), 154 (13), 140 (14), 116 (10). IR (KBr): $\tilde{\nu}$ 3378 (m) cm^{-1}, 1694 (s), 1653 (s), 1627 (s), 1565 (w), 1515 (w), 1443 (m), 1404 (w), 1357 (w), 1231 (w), 1130 (m), 1048 (w), 928 (w), 828 (w), 800 (w), 754 (w), 726 (w), 608 (w), 540 (w). Anal. calcd for $C_{16}H_{14}ClN_3O_2$ (315.8): C 60.86, H 4.47, N 13.31. Found: C 60.93, H 4.71, N 13.11.

4.2.13. 4-(5-(4-Methoxyphenyl)-1*H*-pyrrol-3-yl)pyridine (4m)

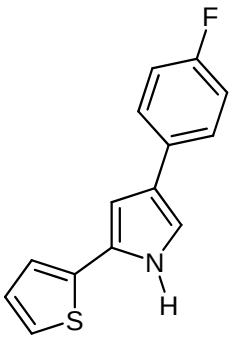


$C_{16}H_{14}N_2O$

250.30

151 mg (0.60 mmol, 60 % yield) as a beige solid. Mp 181-183 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 3.77 (s, 3 H), 6.93-7.00 (m, 3 H), 7.53-7.59 (m, 3 H), 7.60-7.65 (m, 2 H), 8.40-8.45 (m, 2 H), 11.6 (br, 1 H, NH). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 55.0 (CH_3), 102.0 (CH), 114.1 (CH), 118.2 (CH), 118.8 (CH), 121.8 (C_{quat}), 124.9 (CH), 125.1 (C_{quat}), 133.0 (C_{quat}), 142.9 (C_{quat}), 149.6 (CH), 157.7 (C_{quat}). EI + MS (*m/z* (%)): 251 (21), 250 (M^+, 100), 236 (13), 235 ($(M-CH_3)^+$, 89), 207 (39), 206 (20), 205 (15), 180 (11), 179 (11), 178 (13), 153 (11), 152 (35), 151 (18), 128 (11), 127 (15), 126 (12), 125 (11), 102 (10), 89 (13), 77 (19), 76 (12), 63 (15), 51 (15). IR (KBr): $\tilde{\nu}$ 3114 (m) cm^{-1}, 3065 (m), 2991 (m), 2893 (m), 2834 (m), 1602 (s), 1543 (m), 1533 (w), 1505 (s), 1464 (m), 1440 (w), 1429 (m), 1376 (w), 1306 (w), 1287 (m), 1251 (s), 1216 (m), 1180 (m), 1165 (w), 1111 (w), 1094 (w), 1066 (w), 1038 (m), 1001 (m), 935 (w), 834 (m), 795 (s), 750 (w), 738 (w), 691 (m), 667 (w), 638 (w), 610 (w), 525 (m). Anal. calcd for $C_{16}H_{14}N_2O$ (250.3): C 76.78, H 5.64, N 11.19. Found: C 76.51, H 5.80, N 11.20.

4.2.14. 4-(4-Fluorophenyl)-2-(thiophen-2-yl)-1*H*-pyrrole (4n)

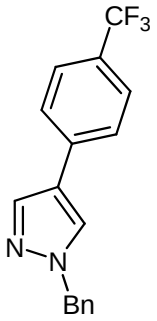


$C_{14}H_{10}FNS$

243.30

170 mg (0.70 mmol, 70 % yield) as a pale gray solid. Mp 163 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.67-6.69 (m, 1 H), 7.05 (dd, *J* = 5.0 Hz, *J* = 3.8 Hz, 1 H), 7.11-7.16 (m, 2 H), 7.26 (dd, *J* = 3.5 Hz, *J* = 0.9 Hz, 1 H), 7.29 (dd, *J* = 2.5 Hz, *J* = 1.9 Hz, 1 H), 7.35 (dd, *J* = 5.0 Hz, *J* = 0.9 Hz, 1 H), 7.58-7.64 (m, 2 H), 11.48 (s, 1 H, N<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 103.3 (CH), 115.2 (d, *J* = 21.1 Hz, CH), 116.1 (CH), 120.9 (CH), 122.7 (CH), 123.5 (C_{quat}), 126.0 (d, *J* = 8.2 Hz, CH), 127.1 (C_{quat}), 127.7 (CH), 131.9 (d, *J* = 2.7 Hz, C_{quat}), 135.9 (C_{quat}), 160.2 (d, *J* = 241.9 Hz, C_{quat}). EI + MS (*m/z* (%)): 244 (18), 243 (M^+, 100), 242 ($(M-H)^+$, 14), 215 (14), 183 (11), 133 (18), 122 (19). IR (KBr): $\tilde{\nu}$ 3412 (s) cm^{-1}, 3123 (w), 1655 (w), 1578 (w), 1535 (w), 1501 (m), 1420 (w), 1300 (w), 1224 (m), 1161 (w), 1130 (m), 1098 (w), 1047 (w), 1010 (w), 924 (w), 840 (s), 811 (w), 793 (s), 770 (m), 685 (s), 662 (m), 597 (w), 577 (w), 538 (m), 515 (s). Anal. calcd for $C_{14}H_{10}FNS$ (243.3): C 69.11, H 4.14, N 5.76. Found: C 69.29, H 4.35, N 5.68.

4.2.15. 1-Benzyl-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (4o)

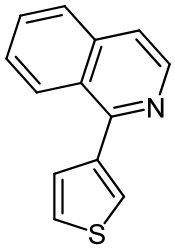


$C_{17}H_{13}F_3N_2$

302.29

106 mg (0.35 mmol, 35 % yield) as a colorless solid. Mp 106 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.35 (s, 2 H), 7.26-7.30 (m, 2 H), 7.31-7.40 (m, 3 H), 7.52-7.56 (m, 2 H), 7.56-7.60 (m, 2 H), 7.67 (s, 1 H), 7.86 (s, 1 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 56.3 (CH_2), 122.2, 124.2 (q, *J* = 272.2 Hz, C_{quat}), 125.4, 125.8 (q, *J* = 3.7 Hz, CH), 126.6, 127.8, 128.2 (q, *J* = 33.0 Hz, C_{quat}), 128.3, 128.9, 136.0, 136.1 (q, *J* = 1.8 Hz, CH), 137.1. EI + MS (*m/z* (%)): 303 (10), 302 (M^+, 49), 301 ($(M-H)^+$, 51), 91 ($C_7H_7^+$, 100), 65 ($C_5H_5^+$, 11). IR (KBr): $\tilde{\nu}$ 3106 (w) cm^{-1}, 2925 (w), 2852 (w), 1620 (m), 1456 (w), 1432 (w), 1337 (s), 1229 (w), 1158 (s), 1113 (s), 1080 (m), 1062 (m), 1000 (w), 953 (w), 842 (m), 729 (m), 693 (w), 597 (w), 510 (w), 453 (w). Anal. calcd for $C_{17}H_{13}F_3N_2$ (302.3): C 67.54, H 4.33, N 9.27. Found: C 67.70, H 4.31, N 9.02.

4.2.16. 1-(Thiophen-3-yl)isoquinoline (4p)



$C_{13}H_9NS$

211.28

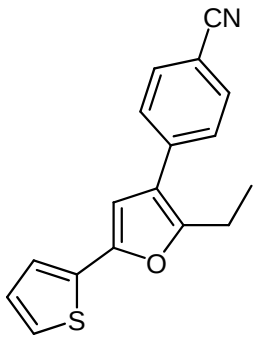
161 mg (0.76 mmol, 76 % yield) as a colorless solid. Mp 91-92 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.49 (dd, *J* = 5.0 Hz, *J* = 2.8 Hz, 1 H), 7.54 (dd, *J* = 5.0 Hz, *J* = 1.3 Hz, 1 H), 7.55-7.59 (m, 1 H), 7.61 (d, *J* = 5.7 Hz, 1 H), 7.67-7.71 (m, 1 H), 7.72 (dd, *J* = 2.8 Hz, *J* = 1.3 Hz, 1 H), 7.87 (d, *J* = 8.2 Hz, 1 H), 8.28 (d, *J* = 8.5 Hz, 1 H), 8.57 (d, *J* = 5.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 119.9 (CH), 125.7 (CH), 126.1 (CH), 126.9 (C_{quat}), 127.0 (CH), 127.2 (CH), 127.3 (CH), 129.2 (CH), 130.0 (CH), 136.8 (C_{quat}), 140.7 (C_{quat}), 142.2 (CH), 155.9 (C_{quat}). EI + MS (*m/z* (%)): 212 (12), 211 (M^+, 57), 210 ($(M-H)^+$, 100), 166 ($C_{12}H_8N^+$, 13), 139 (9), 128 ($C_9H_6N^+$, 3), 84 ($C_4H_4S^+$, 10), 83 ($C_4H_3S^+$, 4). IR (KBr): $\tilde{\nu}$ 3047 (w) cm^{-1}, 1614 (w), 1579 (w), 1552 (m), 1524 (w), 1494 (w), 1452 (w), 1415 (m), 1333 (m), 1306 (m), 1215 (w), 1192 (w), 1138 (w), 1061 (w), 1018 (w), 988 (w), 963 (w), 901 (m), 867 (m), 833 (m), 810 (s), 792 (m), 774 (m), 753 (s), 708 (w), 683 (s), 661 (w), 639 (w), 612 (w), 567 (w), 514 (w). Anal. calcd for $C_{13}H_9NS$ (211.3): C 73.90, H 4.29, N 6.63. Found: C 73.72, H 4.22, N 6.62.

Data reported in the literature:

K. L. Billingsley, T. E. Barder, S. L. Buchwald, *Angew. Chem.* **2007**, *119*, 5455-5459; *Angew. Chem. Int. Ed.* **2007**, *46*, 5359-5363.

Yellow solid. Mp 74-75 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.49 (ddd, *J* = 6 Hz, *J* = 3 Hz, *J* = 1 Hz, 1 H), 7.55 (dt, *J* = 1.6 Hz, 1 H), 7.57 (dt, *J* = 1.8 Hz, 1 H), 7.62 (d, *J* = 6 Hz, 1 H), 7.69 (dt, *J* = 1.8 Hz, 1 H), 7.72 (dt, *J* = 1.3 Hz, 1 H), 7.87 (d, *J* = 8 Hz, 1 H), 8.29 (d, *J* = 8 Hz, 1 H), 8.58 (d, *J* = 6 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 119.8, 125.6, 126.0, 126.9, 127.1, 127.3, 129.1, 130.0, 130.5, 136.7, 140.6, 142.1, 155.8. IR (neat): $\tilde{\nu}$ 3105 cm^{-1}, 3049, 1620, 1582, 1555, 1498, 1418, 1337, 1309. Anal. calcd for $C_{13}H_9NS$ (211.3): C 73.90, H 4.29. Found: C 73.79, H 4.25.

4.2.17. 4-(2-Ethyl-5-(thiophen-2-yl)furan-3-yl)benzonitrile (4q)

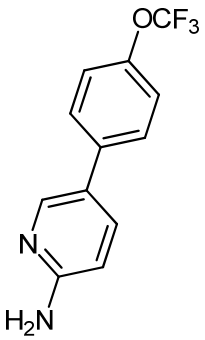


$C_{17}H_{13}NOS$

279.36

221 mg (0.79 mmol, 79 % yield) as a pale yellow solid (after crystallization by suspension in *n*-pentane, sonication in ultrasound bath, filtration and drying in vacuo overnight). Mp 108 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.34 (t, *J* = 7.6 Hz, 3 H), 2.85 (q, *J* = 7.6 Hz, 2 H), 6.60 (s, 1 H), 7.05 (dd, *J* = 5.0 Hz, *J* = 3.8 Hz, 1 H), 7.24 (dd, *J* = 5.0 Hz, *J* = 0.9 Hz, 1 H), 7.27 (dd, *J* = 3.5 Hz, *J* = 0.9 Hz, 1 H), 7.47-7.51 (m, 2 H), 7.66-7.70 (m, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 12.8 (CH_3), 20.6 (CH_2), 105.6 (CH), 110.0 (C_{quat}), 119.0 (C_{quat}), 121.0 (C_{quat}), 122.6 (CH), 124.2 (CH), 127.7 (CH), 128.0 (CH), 132.4 (CH), 133.2 (C_{quat}), 138.7 (C_{quat}), 147.9 (C_{quat}), 153.5 (C_{quat}). EI + MS (*m/z* (%)): 280 (12), 279 (M^+, 59), 265 (18), 264 ($(M\text{-}CH_3)^+$, 100), 166 (22), 164 (17), 131 (13), 129 (13), 111 (23). IR (KBr): $\tilde{\nu}$ 2975 (w) cm^{-1}, 2222 (s), 1606 (s), 1503 (w), 1203 (w), 1177 (w), 1133 (w), 1060 (m), 983 (m), 947 (w), 840 (m), 799 (m), 707 (s), 567 (m), 549 (m). Anal. calcd for $C_{17}H_{13}NOS$ (279.4): C 73.09, H 4.69, N 5.01. Found: C 72.99, H 4.43, N 4.91.

4.2.18. 5-(4-(Trifluoromethoxy)phenyl)pyridin-2-amine (4r)

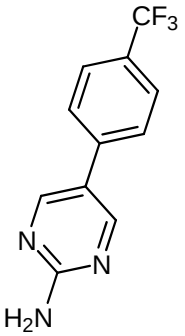


$C_{12}H_9F_3N_2O$

254.21

233 mg (0.92 mmol, 92 % yield) as a colorless solid. Mp 98-101 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.12 (s, 2 H, N$\underline{H}_2$), 6.54 (d, *J* = 8.5 Hz, 1 H), 7.34-7.38 (m, 2 H), 7.65-7.68 (m, 2 H), 7.70 (dd, *J* = 8.5 Hz, *J* = 2.5 Hz, 1 H), 8.24 (d, *J* = 2.5 Hz, 1 H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 108.1 (CH), 120.2 (q, *J* = 255.7 Hz, C_{quat}), 121.6 (CH), 122.6 (C_{quat}), 127.1 (CH), 135.6 (CH), 137.6 (C_{quat}), 146.0 (CH), 147.0 (q, *J* = 1.8 Hz, C_{quat}), 159.5 (C_{quat}). EI + MS (*m/z* (%)): 255 (13), 254 (M^+, 100), 185 ($(M\text{-}CF_3)^+$, 30), 158 (12). IR (KBr): $\tilde{\nu}$ 3490 (w) cm^{-1}, 3466 (w), 3298 (w), 3150 (w), 1638 (s), 1634 (s), 1603 (m), 1562 (w), 1494 (s), 1423 (w), 1389 (m), 1249 (s), 1147 (s), 1017 (w), 997 (w), 857 (w), 827 (w), 806 (w), 671 (w), 537 (w), 509 (w). Anal. calcd for $C_{12}H_9F_3N_2O$ (254.2): C 56.70, H 3.57, N 11.02. Found: C 56.64, H 3.57, N 10.75.

4.2.19. 5-(4-(Trifluoromethyl)phenyl)pyrimidin-2-amine (4s)



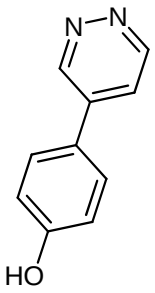
$C_{11}H_8F_3N_3$

239.20

105 mg (0.44 mmol, 44 % yield) as a colorless solid. Mp < 176 °C (subl.)*. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.93 (s, 2 H, N$\underline{H}_2$), 7.73-7.76 (m, 2 H), 7.82-7.86 (m, 2 H), 8.65 (s, 2 H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 120.6 (C_{quat}), 124.5 (q, *J* = 272.2 Hz, C_{quat}), 125.8 (CH), 125.9 (q, *J* = 3.7 Hz, CH), 127.3 (q, *J* = 32.1 Hz, C_{quat}), 139.5 (C_{quat}), 156.5 (CH), 163.3 (C_{quat}). EI + MS (*m/z* (%)): 240 (13), 239 (M^+, 100), 238 ($(M-H)^+$, 26), 211 (10), 198 (13), 170 (28), 169 (12), 151 (12), 120 (17). IR (KBr): $\tilde{\nu}$ 3478 (w) cm^{-1}, 3321 (w), 3165 (w), 1661 (m), 1638 (m), 1599 (m), 1550 (w), 1528 (w), 1482 (m), 1424 (w), 1382 (w), 1324 (s), 1300 (m), 1224 (w), 1174 (m), 1133 (m), 1112 (m), 1071 (m), 1013 (w), 838 (m), 799 (w), 721 (w), 664 (w), 639 (w), 599 (w), 517 (w). Anal. calcd for $C_{11}H_8F_3N_3$ (239.2): C 55.23, H 3.37, N 17.57. Found: C 55.23, H 3.44, N 17.46.

*Slow sublimation with not clearly detectable sublimation point.

4.2.20. 4-(Pyridazin-4-yl)phenol (4t)



$C_{10}H_8N_2O$

172.18

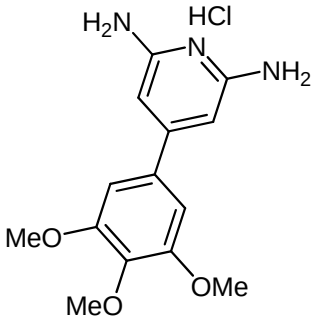
121 mg (0.70 mmol, 70 % yield) as a rosa solid. Mp 242 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.91-6.95 (m, 2 H), 7.76-7.80 (m, 2 H), 7.88 (dd, *J* = 5.4 Hz, *J* = 2.5 Hz, 1 H), 9.14 (dd, *J* = 5.4 Hz, *J* = 1.3 Hz, 1 H), 9.55 (dd, *J* = 2.5 Hz, *J* = 1.3 Hz, 1 H), 10.2 (br, 1 H, O<u>H</u>). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 116.4 (CH), 122.0 (CH), 124.2 (C_{quat}), 128.7 (CH), 137.2 (C_{quat}), 149.0 (CH), 151.5 (CH), 159.6 (C_{quat}). EI + MS (*m/z* (%)): 173 (13), 172 (M^+, 100), 118 (41), 115 (30), 91 (10), 89 (16). IR (KBr): $\tilde{\nu}$ 3448 (w) cm^{-1}, 3073 (w), 1615 (w), 1574 (s), 1515 (m), 1444 (w), 1390 (w), 1360 (w), 1285 (s), 1242 (w), 1177 (m), 1111 (w), 1046 (w), 979 (w), 839 (w), 812 (m), 789 (w), 745 (w), 665 (w), 571 (w). Anal. calcd for $C_{10}H_8N_2O$ (172.2): C 69.76, H 4.68, N 16.27. Found: C 69.49, H 4.91, N 16.10.

Data reported in the literature:

R. Stoermer, O. Gaus, *Ber. dtsch. Chem. Ges.* **1912**, *45*, 3104-3113.

Long colorless needles (EtOH). Mp 242 °C. Anal. calcd for $C_{10}H_8N_2O$ (172.2): N 15.92. Found: N 16.23.

4.2.21. 4-(3,4,5-Trimethoxyphenyl)pyridine-2,6-diamine hydrochloride (4u)



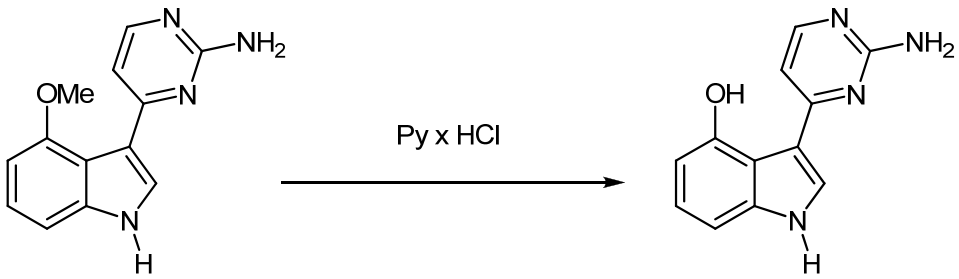
$C_{14}H_{18}ClN_3O_3$

311.76

136 mg (0.44 mmol, 44 % yield) as an orange solid (after crystallization with *n*-pentane from 1.25 *M* HCl in EtOH, filtration, washing with *n*-pentane, and drying in vacuo overnight at 70 °C). Mp 128-135 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 1.34 (t, *J* = 7.6 Hz, 3 H), 2.85 (q, *J* = 7.6 Hz, 2 H), 6.60 (s, 1 H), 7.05 (dd, *J* = 5.0 Hz, *J* = 3.8 Hz, 1 H), 7.24 (dd, *J* = 5.0 Hz, *J* = 0.9 Hz, 1 H), 7.27 (dd, *J* = 3.5 Hz, *J* = 0.9 Hz, 1 H), 7.47-7.51 (m, 2 H), 7.66-7.70 (m, 2 H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 12.8 (CH_3), 20.6 (CH_2), 105.6 (CH), 110.0 (C_{quat}), 119.0 (C_{quat}), 121.0 (C_{quat}), 122.6 (CH), 124.2 (CH), 127.7 (CH), 128.0 (CH), 132.4 (CH), 133.2 (C_{quat}), 138.7 (C_{quat}), 147.9 (C_{quat}), 153.5 (C_{quat}). EI + MS (*m/z* (%)): 276 (17), 275 ((M-HCl)$^+$, 100), 260 ((M-HCl-CH_3)$^+$, 17), 217 ($C_{11}H_{11}N_3O_2^+$, 20), 108 ($C_5H_6N_3^+$, 5). IR (KBr): $\tilde{\nu}$ 3410 (m) cm^{-1}, 3334 (m), 3207 (m), 2941 (w), 2837 (w), 2741 (w), 1645 (s), 1588 (m), 1518 (w), 1492 (w), 1463 (w), 1413 (w), 1378 (m), 1325 (m), 1267 (w), 1245 (w), 1169 (w), 1127 (s), 999 (m), 965 (w), 831 (w), 807 (w), 757 (w), 720 (w), 562 (w), 524 (w). Anal. calcd for $C_{14}H_{18}ClN_3O_3$ (311.8): C 53.93, H 5.82, N 13.48. Found: C 53.73, H 6.03, N 13.35.

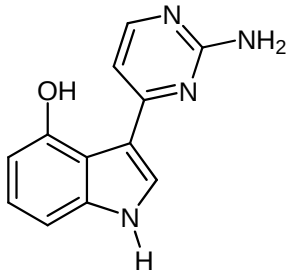
4.3. Synthesis of Meridianin A (5)

Synthesis of 3-(2-aminopyrimidin-4-yl)-1*H*-indol-4-ol (*Meridianin A*, 5*)*



Pyridinium hydrochloride (1.18 g, 10.0 mmol) was placed in a dry screw-cap vessel under argon atmosphere. Then, 4-(4-methoxy-1*H*-indol-3-yl)pyrimidin-2-amine (**4j**) (120 mg, 0.50 mmol) was added and the mixture was heated to 210 °C (preheated oil bath). After 30 min, the mixture was cooled to 50 °C (preheated oil bath) and methanol was added to dissolve the residue. The reaction mixture was monitored by TLC. The mixture was adsorbed on Celite® and the solvents were removed under reduced pressure. The residue was purified chromatographically on silica gel with dichloromethane-methanol-aqueous ammonia DCM-MeOH-NH_3 = 100:1:1 → 100:2:1 → 100:3:1→ 100:4:1 (stepwise gradient). After drying in vacuo, *meridianin A* (**5**) was obtained as a bright yellow fine crystalline solid.

Spectroscopic data of 3-(2-aminopyrimidin-4-yl)-1*H*-indol-4-ol (*Meridianin A*, 5)



$C_{12}H_{10}N_4O$

226.23

96 mg (0.43 mmol, 85 % yield) as a bright yellow fine crystalline solid. Mp 264-276 °C. (Lit.: 164-168 °C). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 6.39 (dd, *J* = 7.9 Hz, *J* = 0.9 Hz, 1 H), 6.76 (s, 2 H, N$\underline{H}_2$), 6.82 (dd, *J* = 8.2 Hz, *J* = 0.9 Hz, 1 H), 7.00 (t, *J* = 7.9 Hz, 1 H), 7.14 (d, *J* = 5.4 Hz, 1 H), 8.14 (d, *J* = 5.4 Hz, 1 H), 8.25 (d, *J* = 3.2 Hz, 1 H), 11.8 (br, 1 H, N$\underline{H}$), 13.62 (s, 1 H, O$\underline{H}$). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 102.3 (CH), 104.3 (CH), 105.5 (CH), 113.7 (C_{quat}), 114.3 (C_{quat}), 124.4 (CH), 128.4 (CH), 139.2 (C_{quat}), 152.0 (C_{quat}), 158.4 (CH), 160.4 (C_{quat}), 161.7 (C_{quat}). EI + MS (*m/z* (%)): 226 (M^+, 100), 225 ($(M-H)^+$, 13), 209 ($(M-OH)^+$, 2), 197 ($(M-COH)^+$, 6), 185 ($(M-CH_2N_2+H)^+$, 18), 158 ($(M-C_3H_4N_2)^+$, 6). IR (KBr): $\tilde{\nu}$ 3429 (m) cm^{-1}, 3342 (m), 1638 (m), 1593 (s), 1562 (m), 1532 (m), 1469 (m), 1444 (m), 1401 (m), 1321 (m), 1272 (w), 1227 (m), 1194 (w), 1167 (w), 820 (w), 802 (w), 775 (w), 719 (m), 617 (w). Anal. calcd for $C_{12}H_{10}N_4O$ (226.2): C 63.71, H 4.46, N 24.76. Found: C 63.48, H 4.61, N 24.72.

The NMR spectra are in good agreement with reported spectra of *psammopemmin A* (M. S. Butler, R. J. Capon, C. C. Lu, *Austr. J. Chem.* **1992**, *45*, 1871-1877), which might confer the structure reassignment of *psammopemmin A* by *Baker* (M. D. Lebar, B. J. Baker, *Austr. J. Chem.* **2010**, *63*, 862-866).

^{1}H NMR (DMSO-d_6, 400 MHz): δ 6.38 (dd, *J* = 0.7 Hz, *J* = 0.7 Hz, 1 H), 6.68 (br s, 2 H, N$\underline{H}_2$), 6.81 (dd, *J* = 7.7 Hz, *J* = 0.7 Hz, 1 H), 6.98 (dd, *J* = 7.7 Hz, *J* = 7.7 Hz, 1 H), 7.12 (d, *J* = 5.4 Hz, 1 H), 8.12 (br d, *J* = 5.4 Hz, 1 H), 8.22 (d, *J* = 2.5 Hz, 1 H), 11.75 (br s, 1 H, N$\underline{H}$), 13.55 (s, 1 H, O$\underline{H}$). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 102.3, 104.3, 105.4, 113.7, 114.3, 124.3, 128.3, 139.2, 152.0, 158.3, 160.7, 161.7.

Data reported in the literature:

L. H. Franco, E. Bal de Kier Joffé, L. Puricelli, M. Tatian, A. M. Seldes, J. A. Palermo, *J. Nat. Prod.* **1998**, *61*, 1130-1132.

Yellow needles (MeOH-H_2O). Mp 164-168 °C. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 6.36 (dd, *J* = 7.1 Hz, *J* = 0.7 Hz, H-5), 6.69 (s, N$\underline{H}_2$), 6.78 (dd, *J* = 7.5 Hz, *J* = 0.7 Hz, H-7), 6.96 (dd, *J* = 7.5 Hz, *J* = 7.1 Hz, H-6), 7.09 (d, *J* = 5.4 Hz, H-5´), 8.10 (d, *J* = 5.4 Hz, H-6´), 8.20 (d, *J* = 1.2 Hz, H-2), 11.71 (brs, N$\underline{H}$), 13.55 (s, O$\underline{H}$). ^{13}C NMR (DMSO-d_6, 50 MHz): δ 102.4 (C-7), 104.5 (C-5´), 105.6 (C-5), 113.8 (C-3), 114.5 (C-3a), 124.4 (C-6), 128.5 (C-2), 139.4 (C-7a), 152.1 (C-4), 158.5 (C-6´), 160.6 (C-4´), 161.9 (C-2´). HREIMS calcd for $C_{12}H_{10}N_4O$: 226.0855. Found: 226.0857. IR (KBr): $\tilde{\nu}$ 3437 cm^{-1}, 3351, 3200, 2924, 1647, 1605, 1533, 1469, 1326, 820, 721. UV (CH_3Cl) γ_{max} (logε) 248 (3.68), 356 (3.58) nm.

NMR spectra of *meridianin A* are in good agreement with those given by *Palermo*.

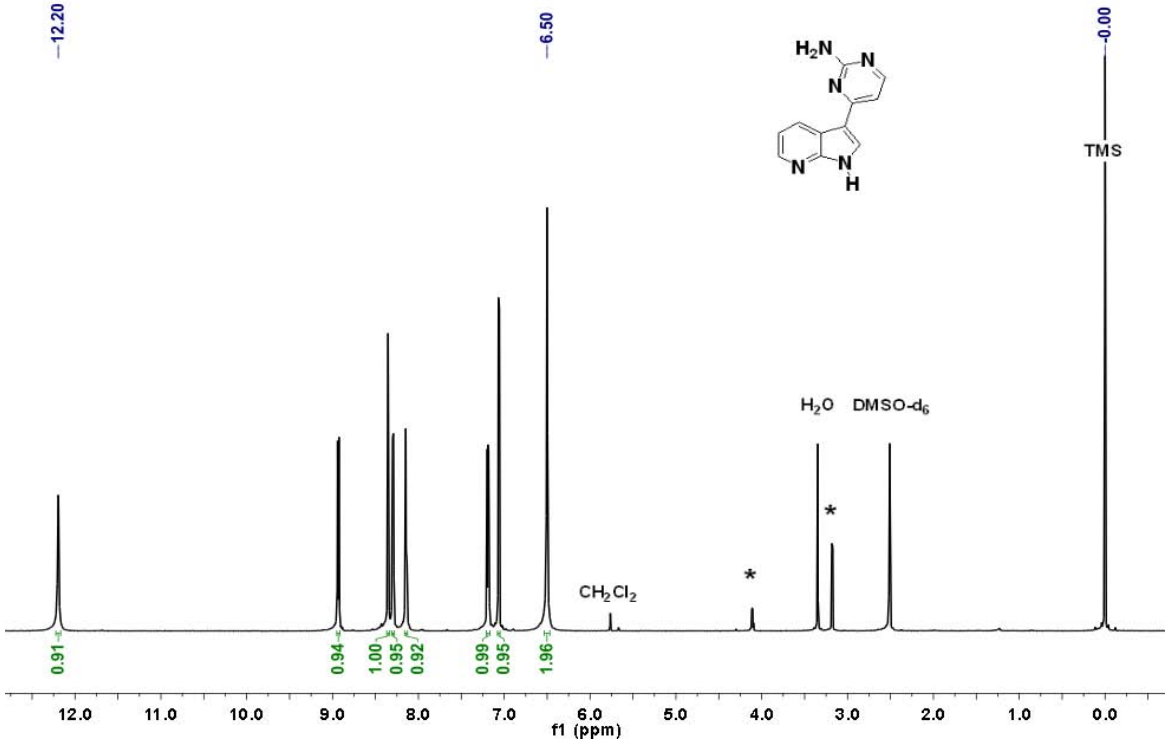
P. M. Fresneda, P. Molina, J. A. Bleda, *Tetrahedron* **2001**, *57*, 2355-2363.

Yellow prisms (EtOH-hexane). Mp 164-168 °C. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.13 (dd, *J* = 7.8 Hz, *J* = 0.9 Hz, 1 H, H-5), 7.48 (brs, 2 H, N$\underline{H}_2$), 7.57 (dd, *J* = 8.1 Hz, *J* = 0.9 Hz, 1 H), 7.74 (dd, *J* = 7.8 Hz, 1 H, H-6), 7.88 (d, *J* = 5.7 Hz, 1 H, H-5´), 8.88 (d, *J* = 5.7 Hz, 1 H, H-6´), 9.0 (s, 1 H, H-2), 11.8 (s, 1 H, N$\underline{H}$), 13.9 (s, 1 H, O$\underline{H}$). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 102.3 (C-7), 104.4 (C-5´), 105.4 (C-5), 113.7 (C-3), 114.4 (C-3a), 124.4 (C-6), 128.4 (C-2), 139.2 (C-7a), 152.0 (C-4), 158.4 (C-6´), 160.5 (C-4´), 161.7 (C-2´). IR (nujol): $\tilde{\nu}$ 3456 (m) cm^{-1}, 3416 (m), 3340 (m), 3181 (m), 1627 (m), 1586 (s), 1532 (s), 1270 (s), 1124 (s), 1072 (s). EI + MS (*m/z* (%)): 226 (M^+, 100), 185 (26), 167 (16), 149 (59). Anal. calcd for $C_{12}H_{10}N_4O$ (226.2): C 63.71, H 4.46, N 24.76. Found: C 63.57, H 4.31, N 24.93.

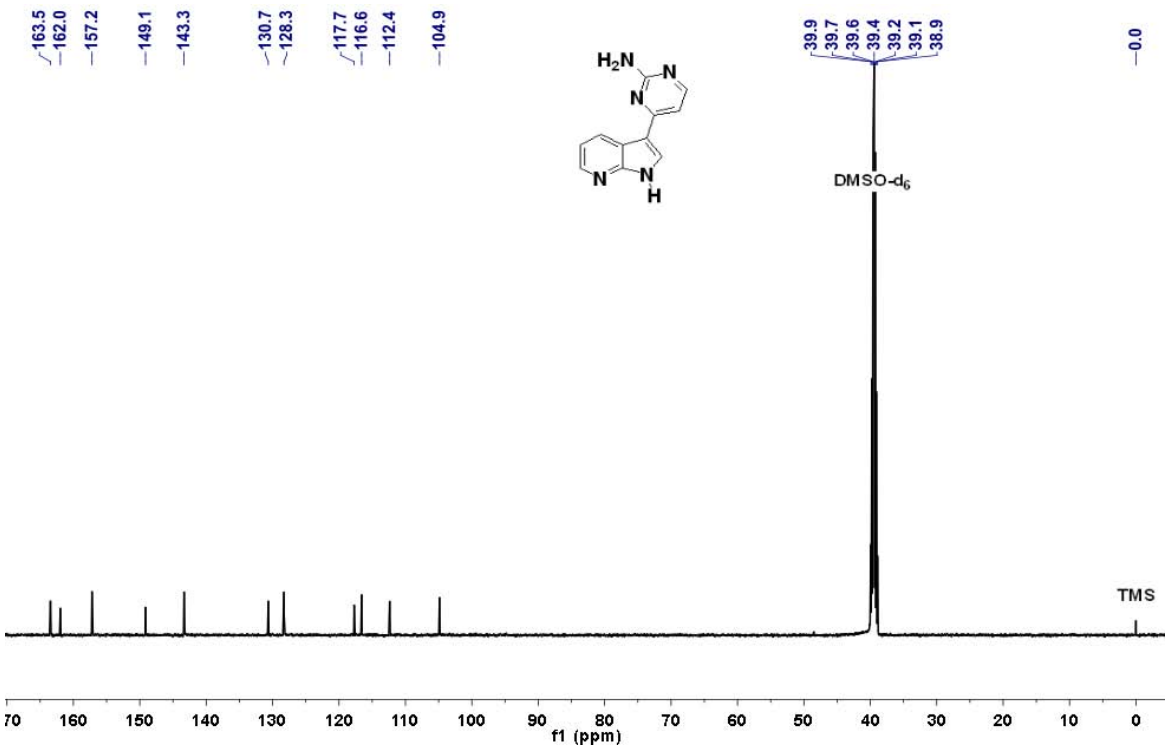
The ^{13}C NMR values are in good agreement with those given by *Fresneda* and *Molina*, but the ^{1}H NMR values deviate considerably.

However, the melting point deviates immensely from the melting point reported both by *Palermo* as well as *Fresneda* and *Molina*.

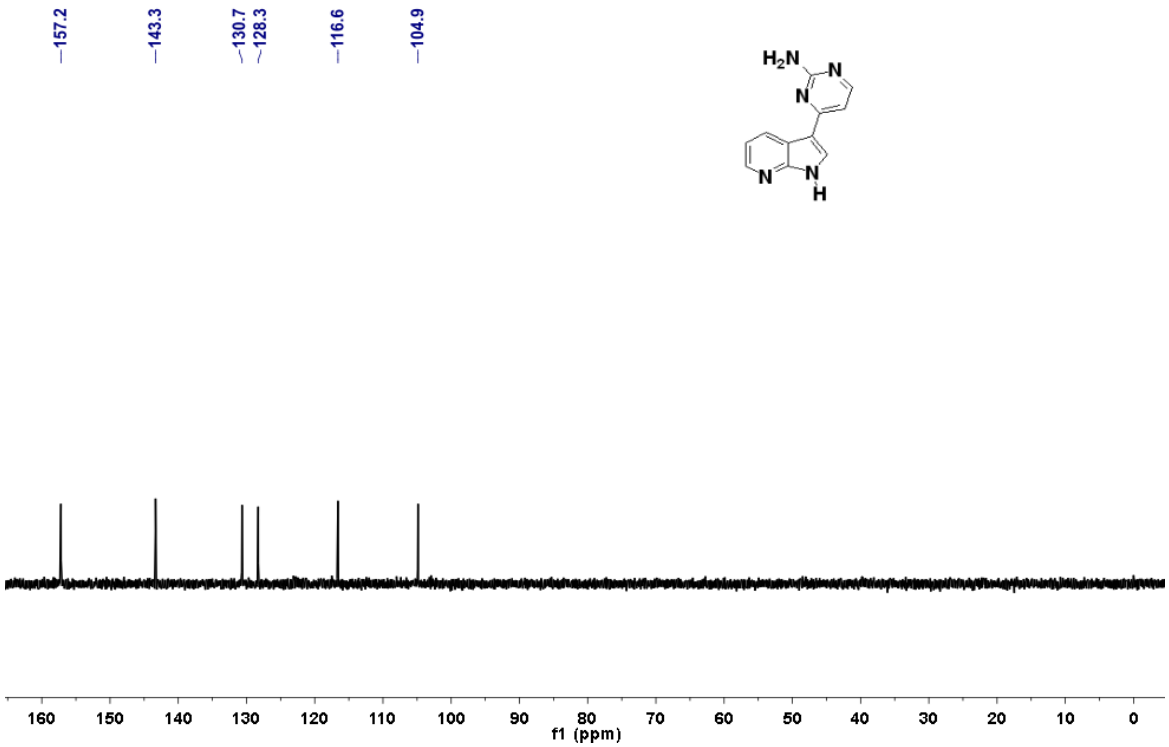
5. ^{1}H and ^{13}C NMR Spectra of Compounds 4a-u and 5



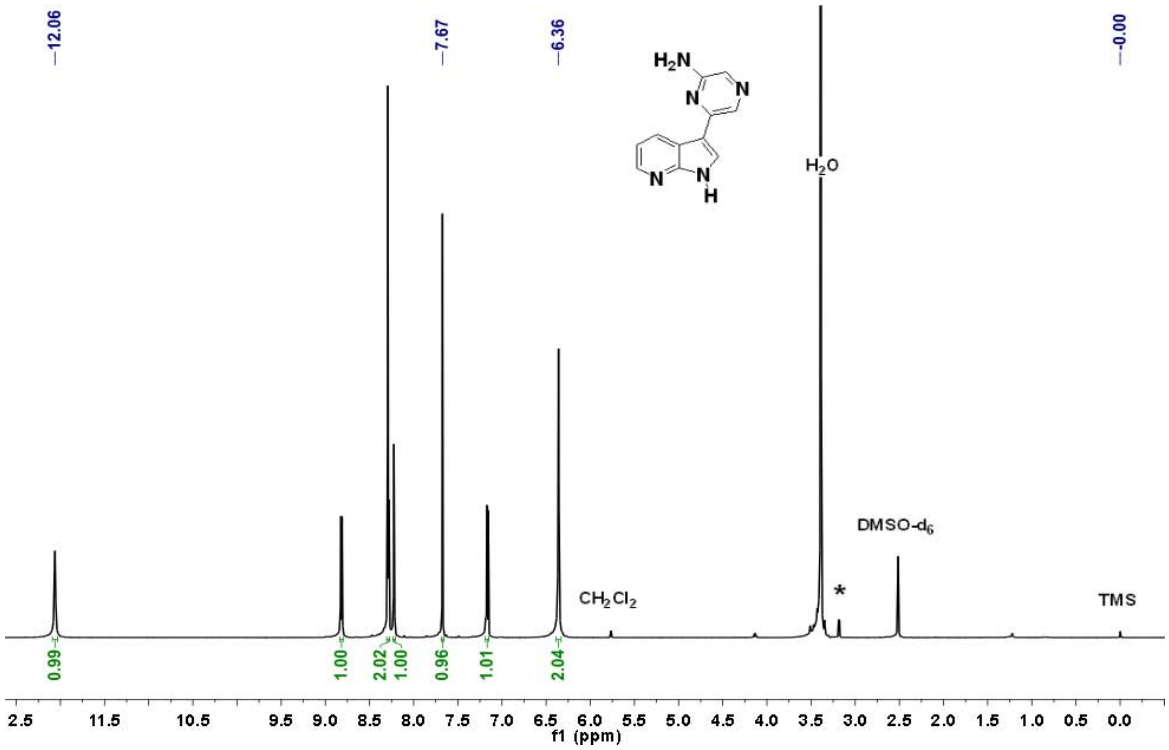
^{1}H NMR of **4a** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm). *Impurities from residual solvents.



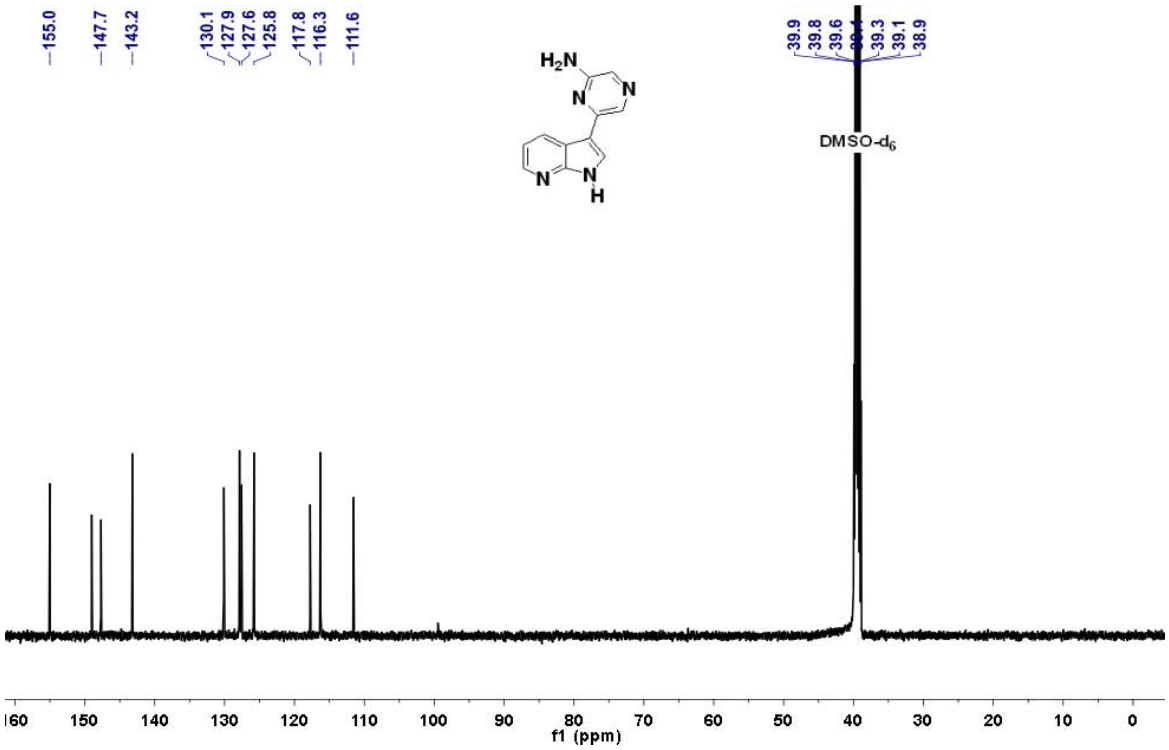
^{13}C NMR of **4a** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



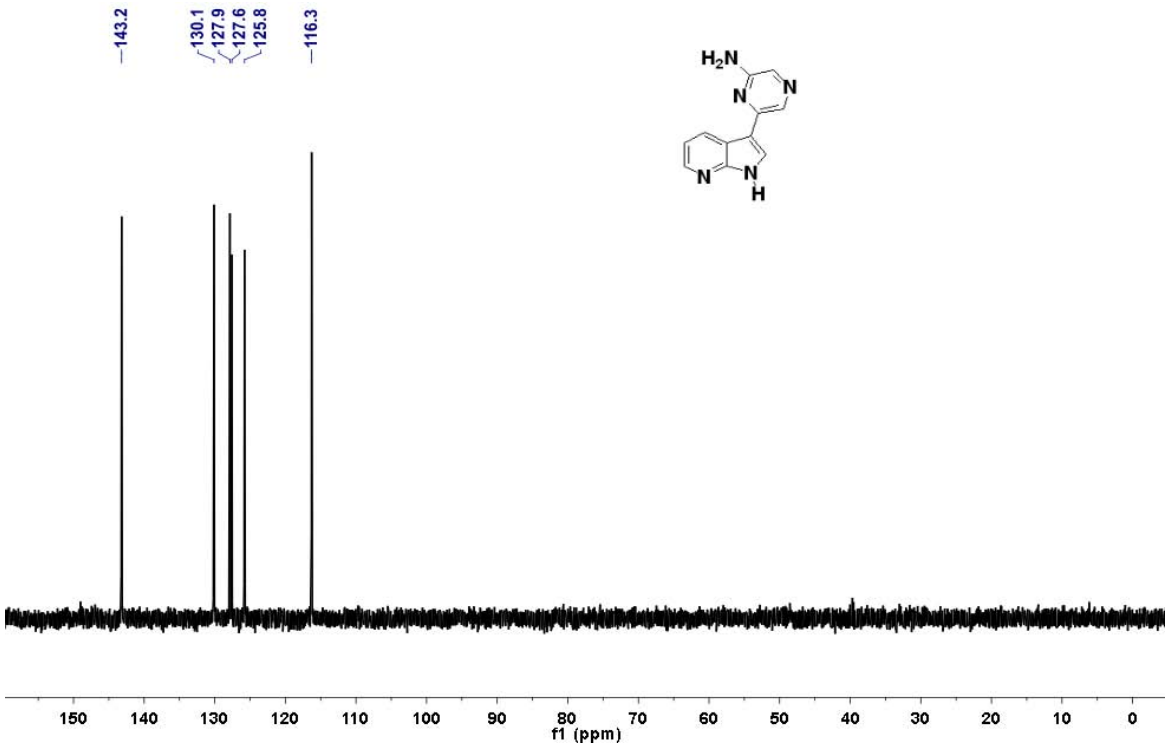
^{13}C DEPT 135-NMR of **4a** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



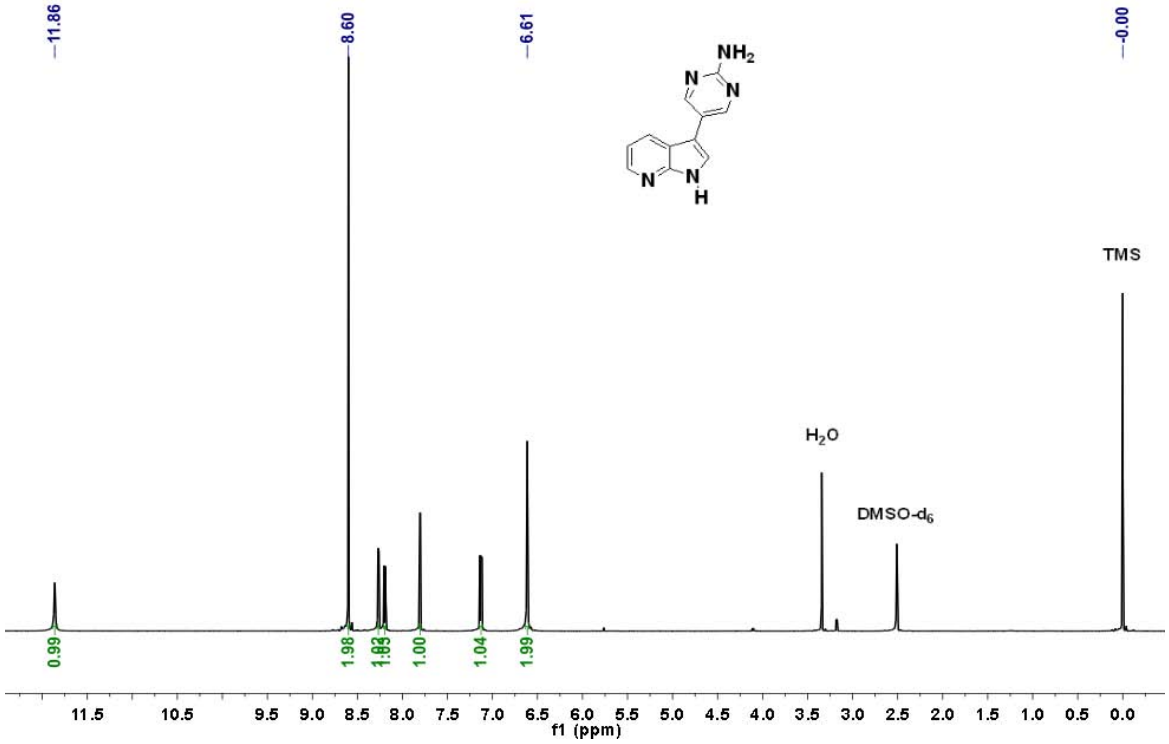
^{1}H NMR of **4b** (15 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm). *Impurities from residual solvents.



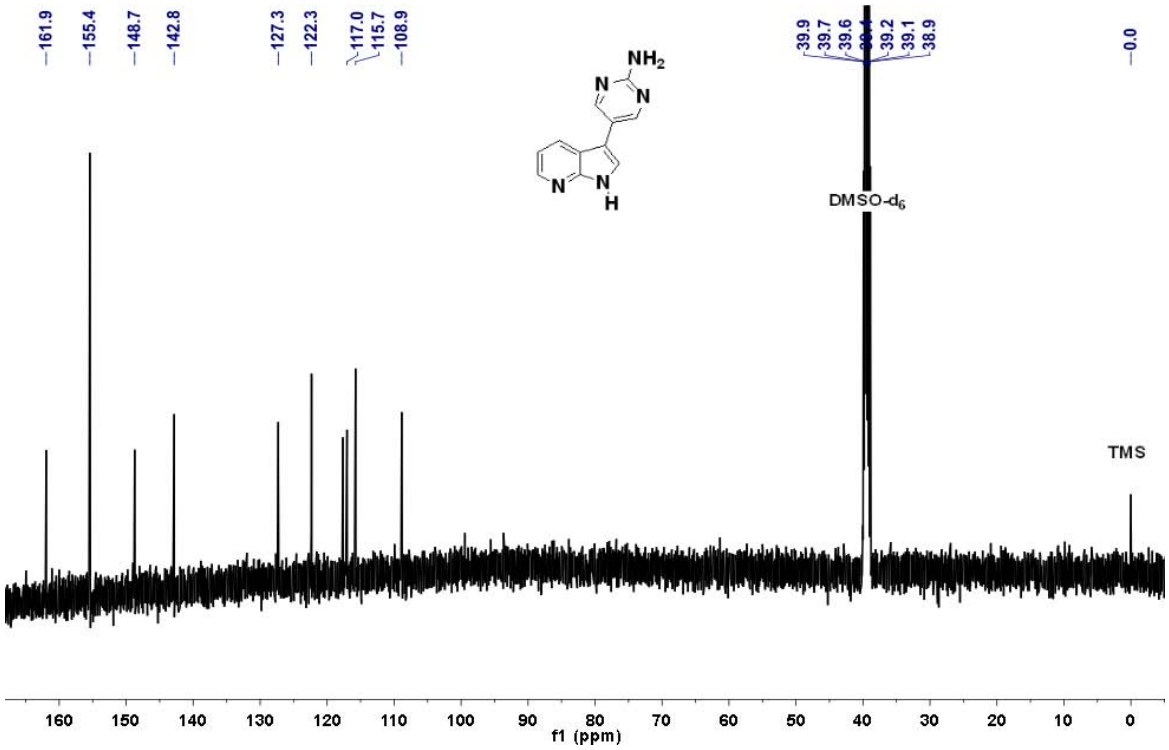
^{13}C NMR of **4b** (15 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



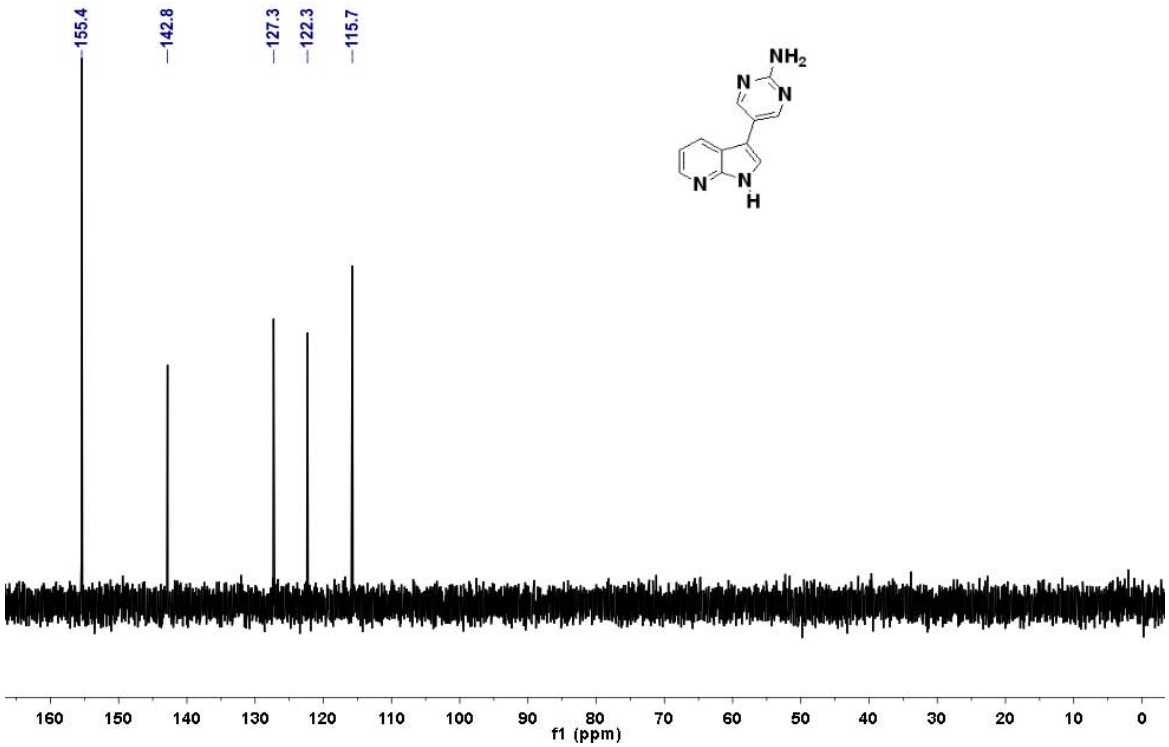
^{13}C DEPT 135-NMR of **4b** (15 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



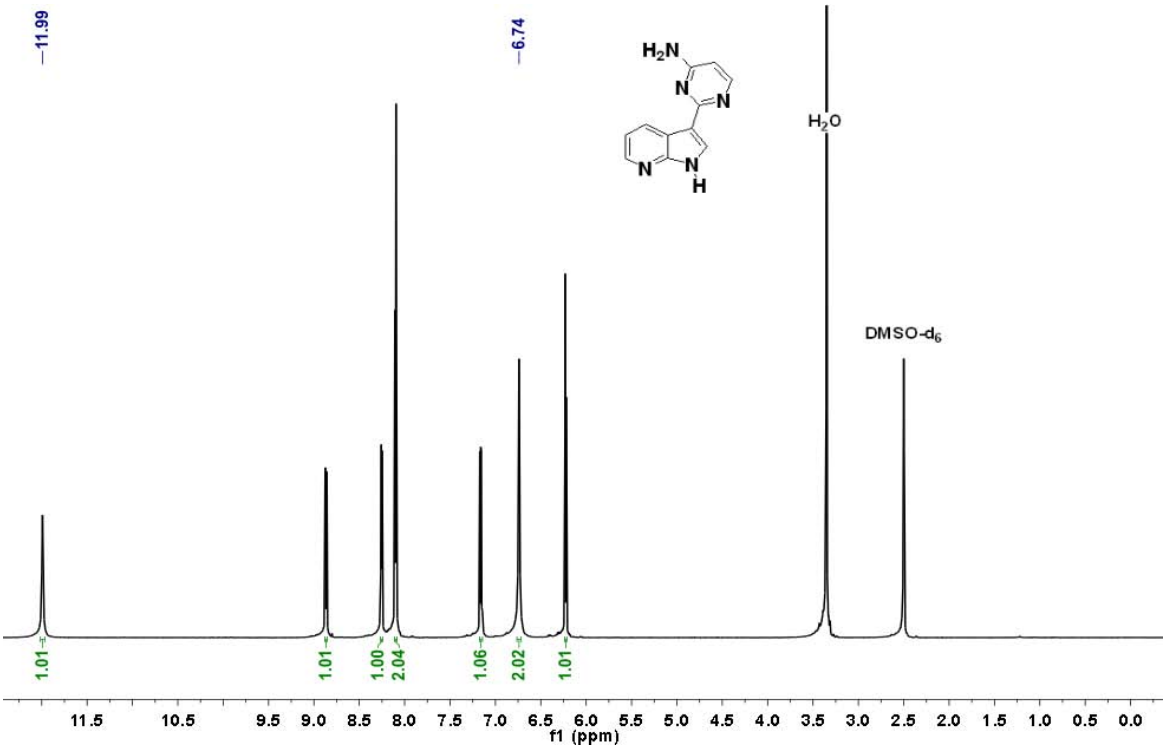
^{1}H NMR of **4c** (15 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



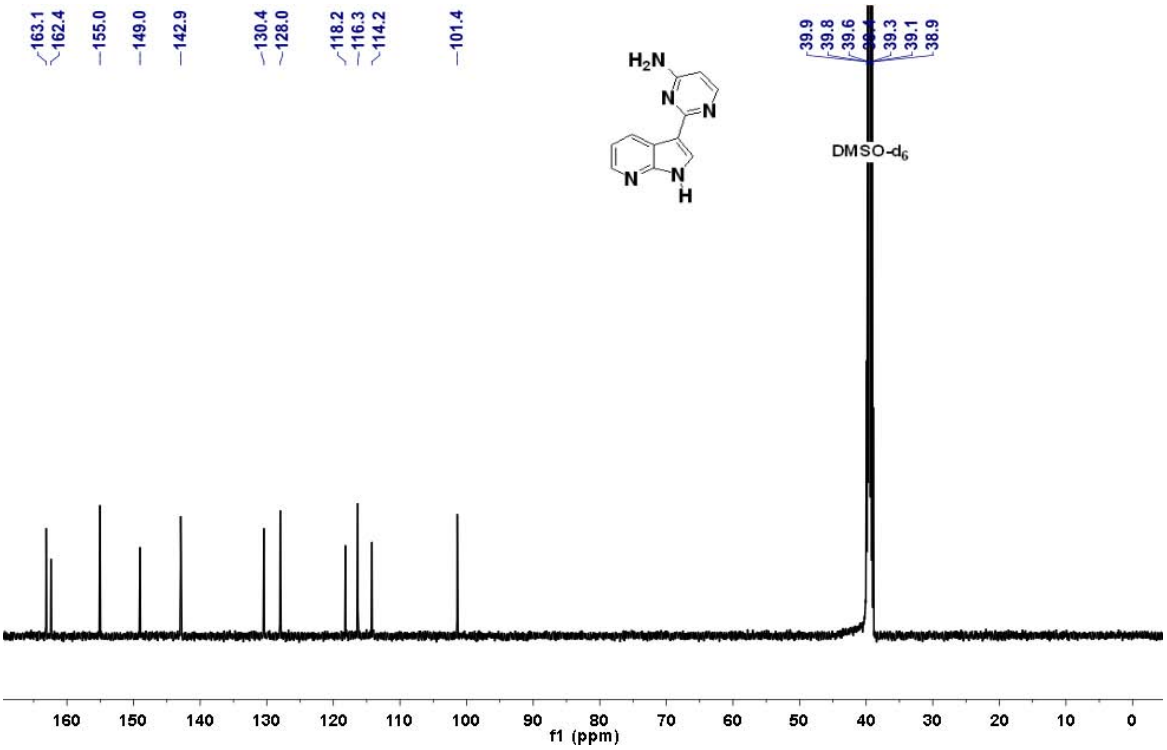
^{13}C NMR of **4c** (15 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



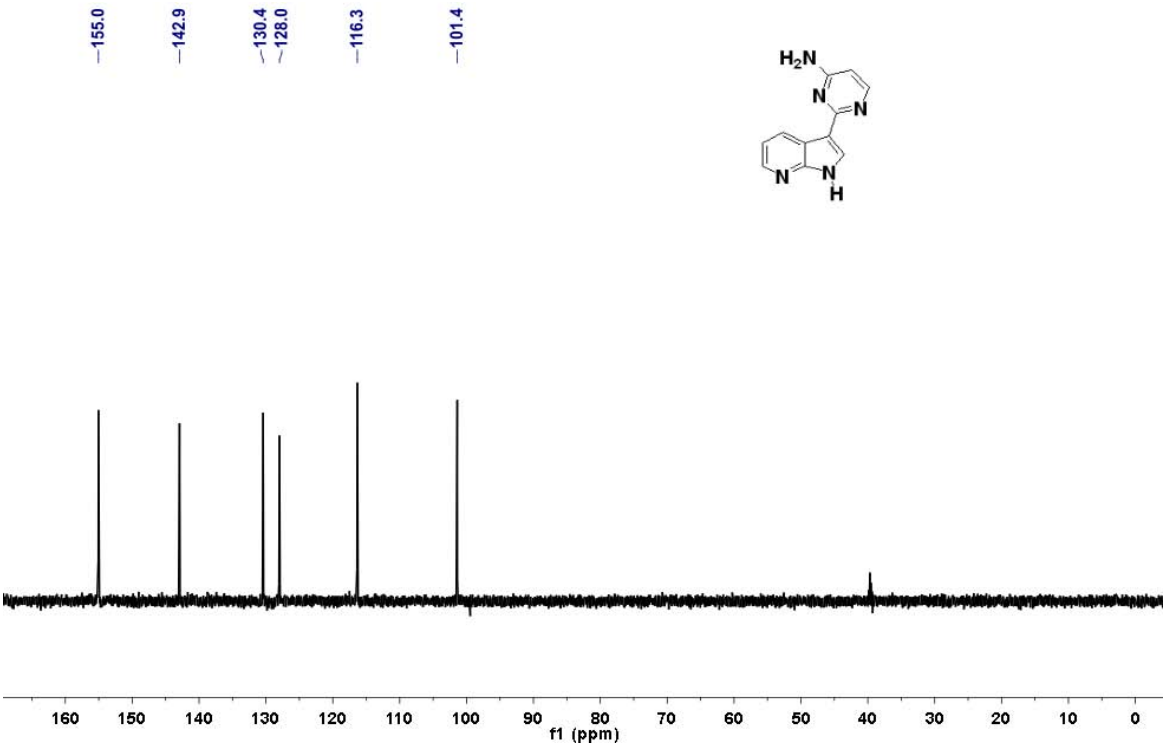
^{13}C DEPT 135-NMR of **4c** (15 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



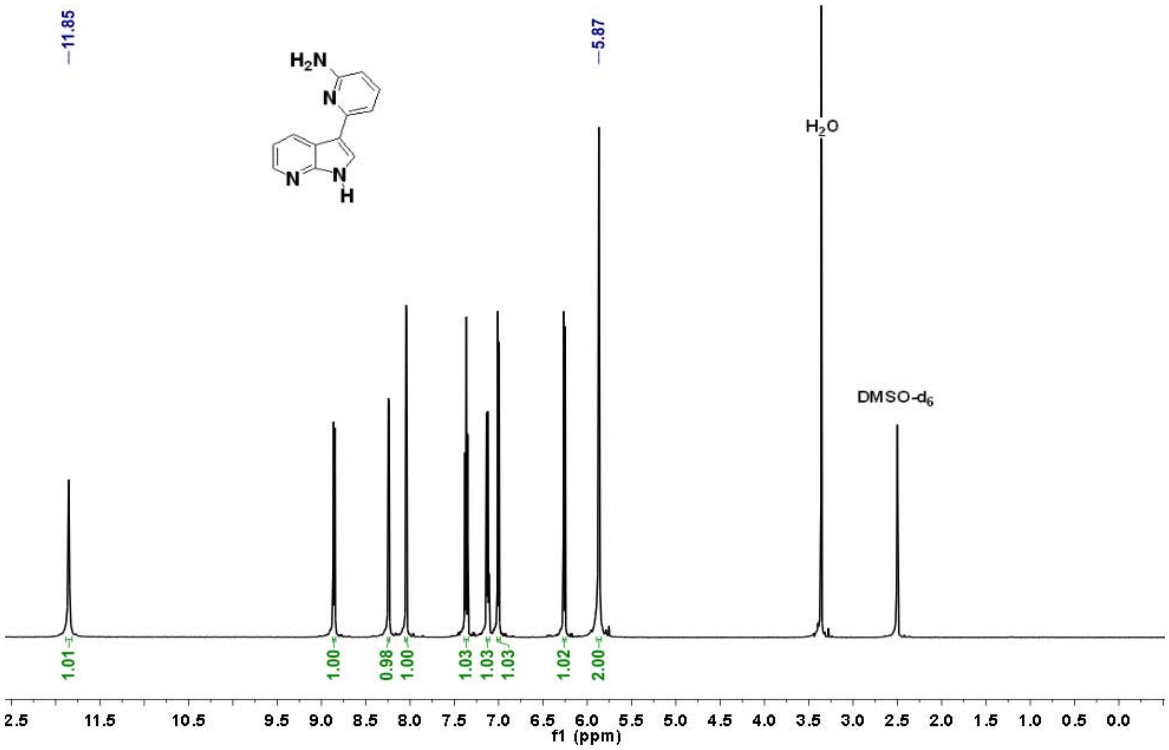
^{1}H NMR of **4d** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



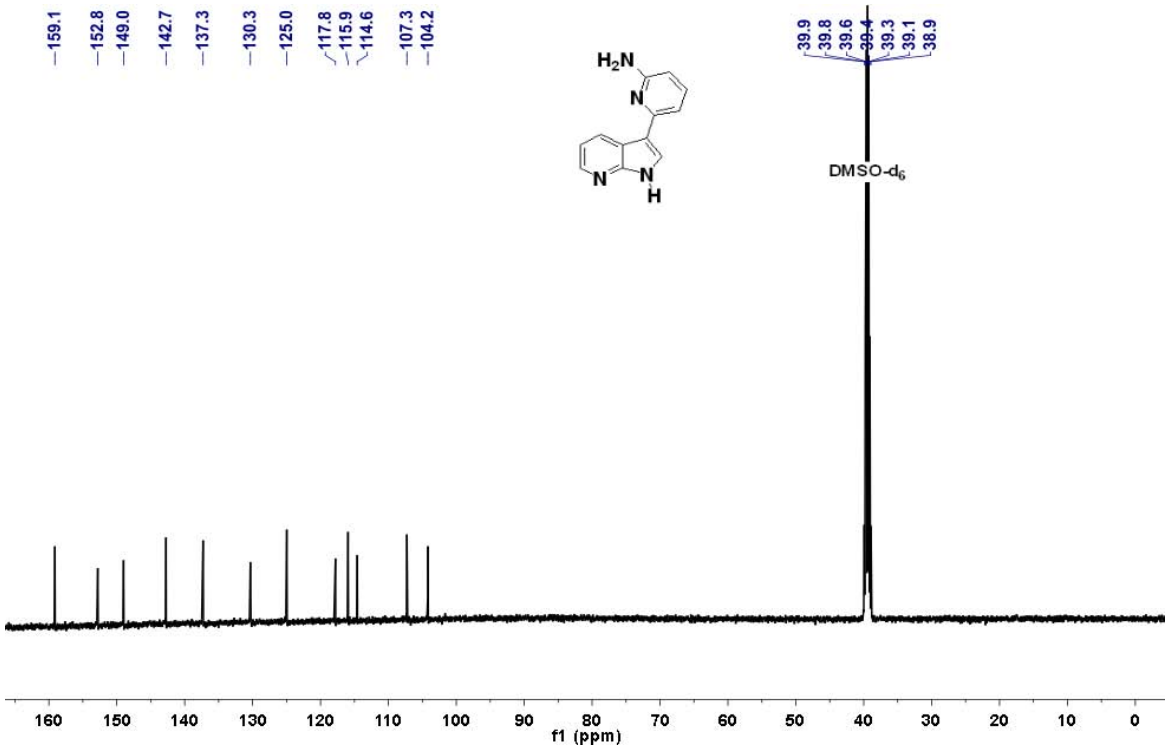
^{13}C NMR of **4d** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



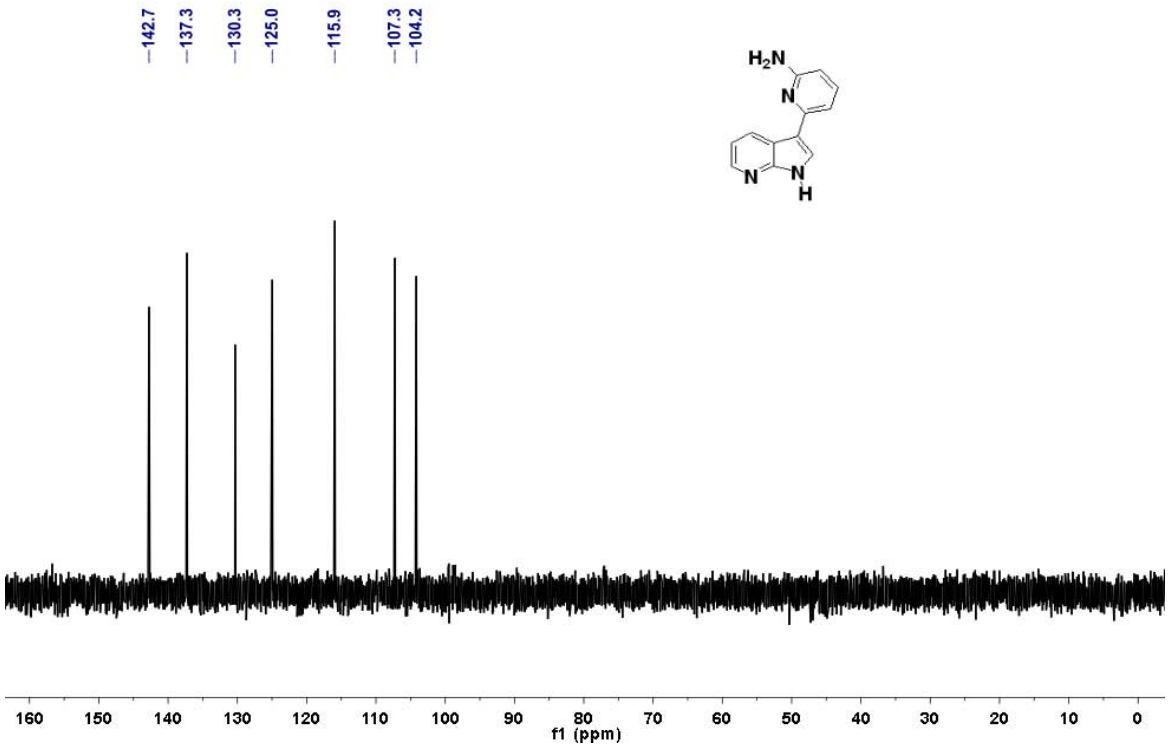
^{13}C DEPT 135-NMR of **4d** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



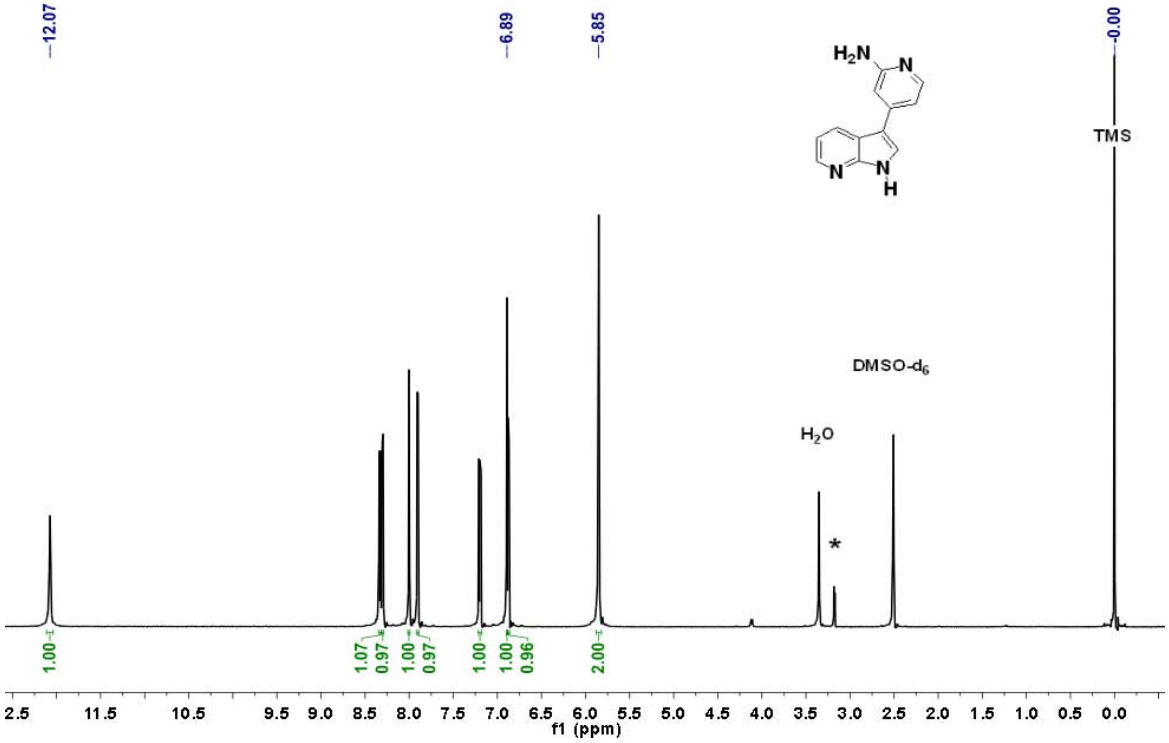
^{1}H NMR of **4e** (15 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



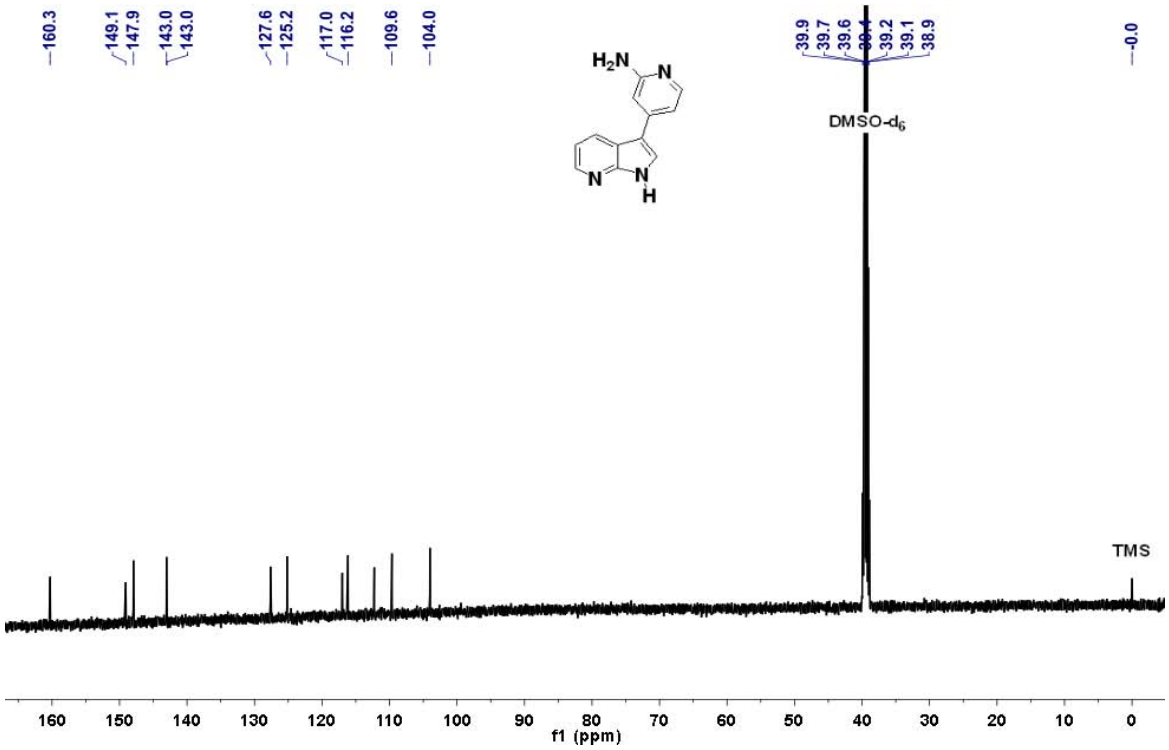
^{13}C NMR of **4e** (15 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



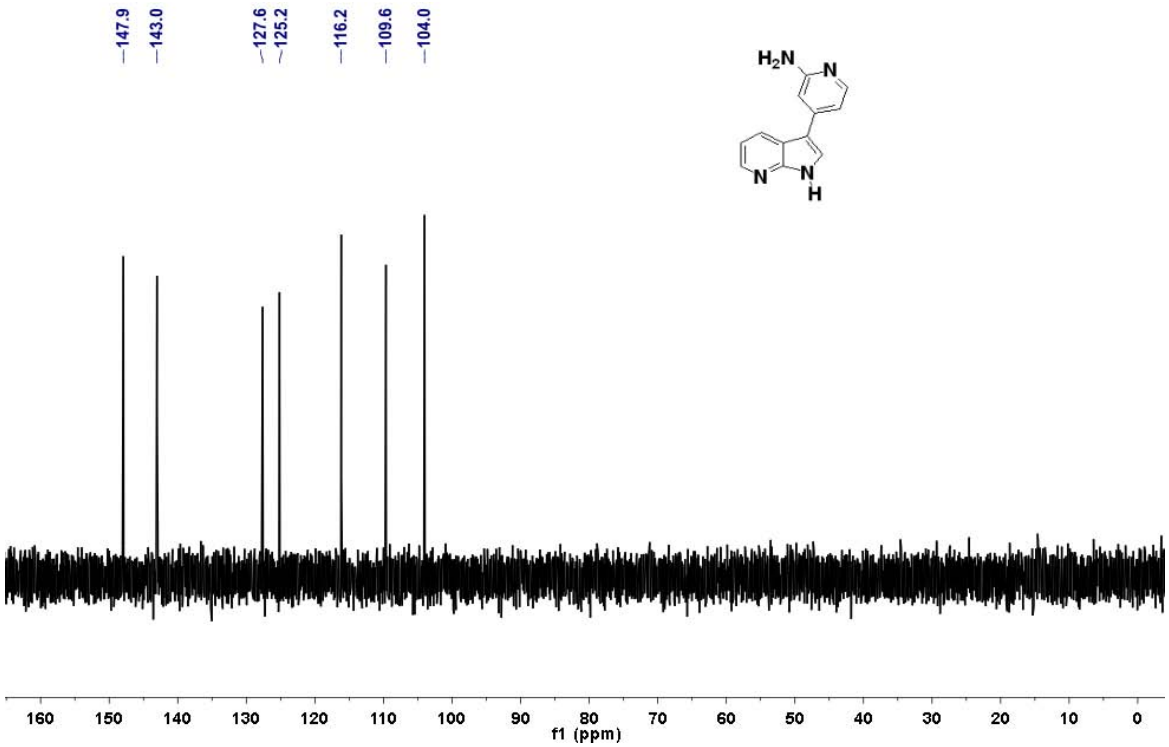
^{13}C DEPT 135-NMR of **4e** (15 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



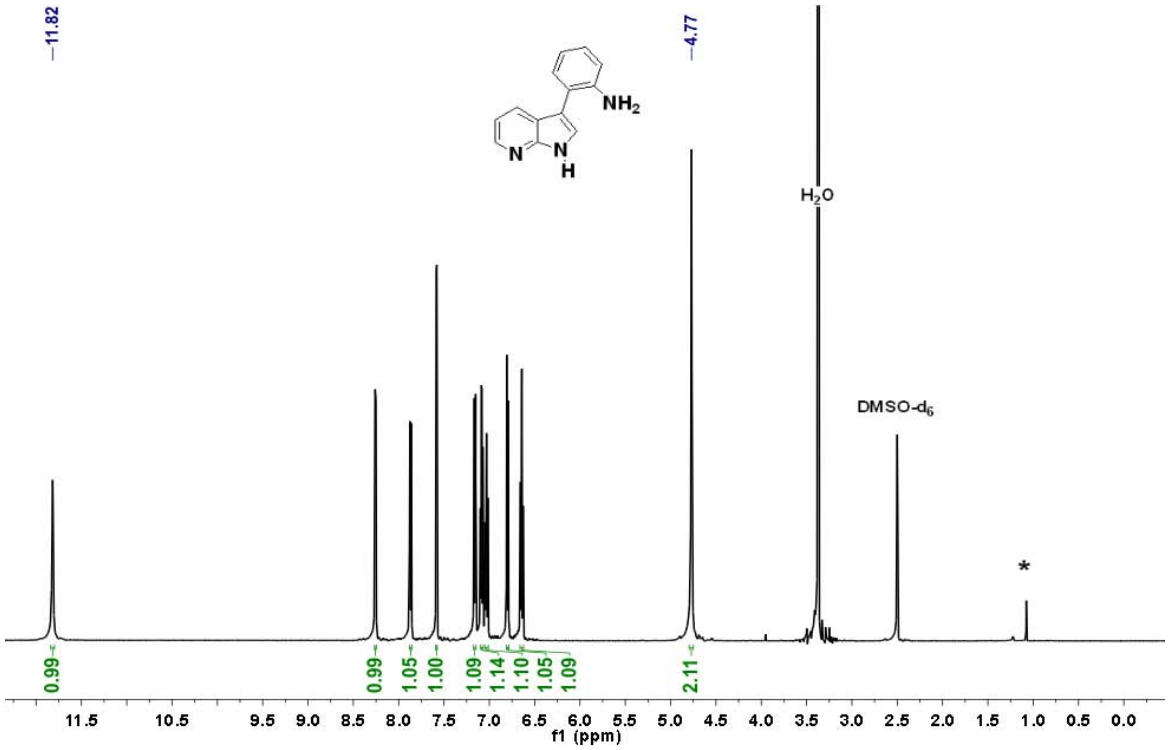
^{1}H NMR of **4f** (15 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm). *Impurities from residual solvents.



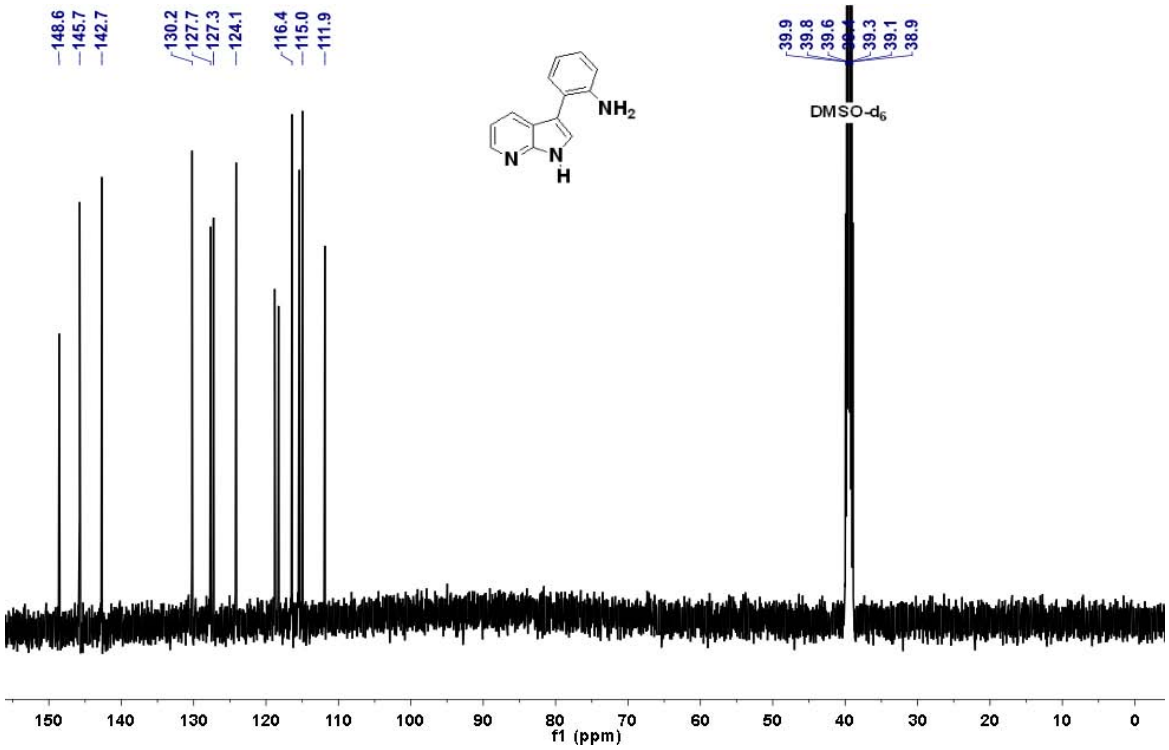
^{13}C NMR of **4f** (15 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



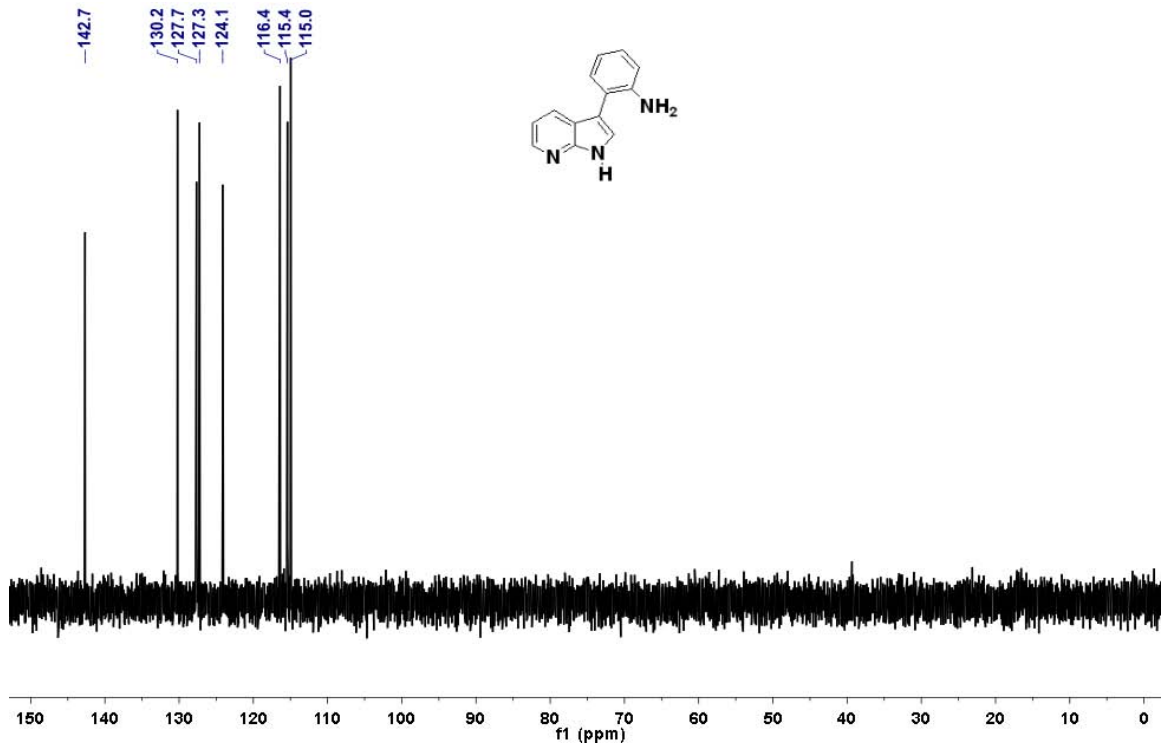
^{13}C DEPT 135-NMR of **4f** (15 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



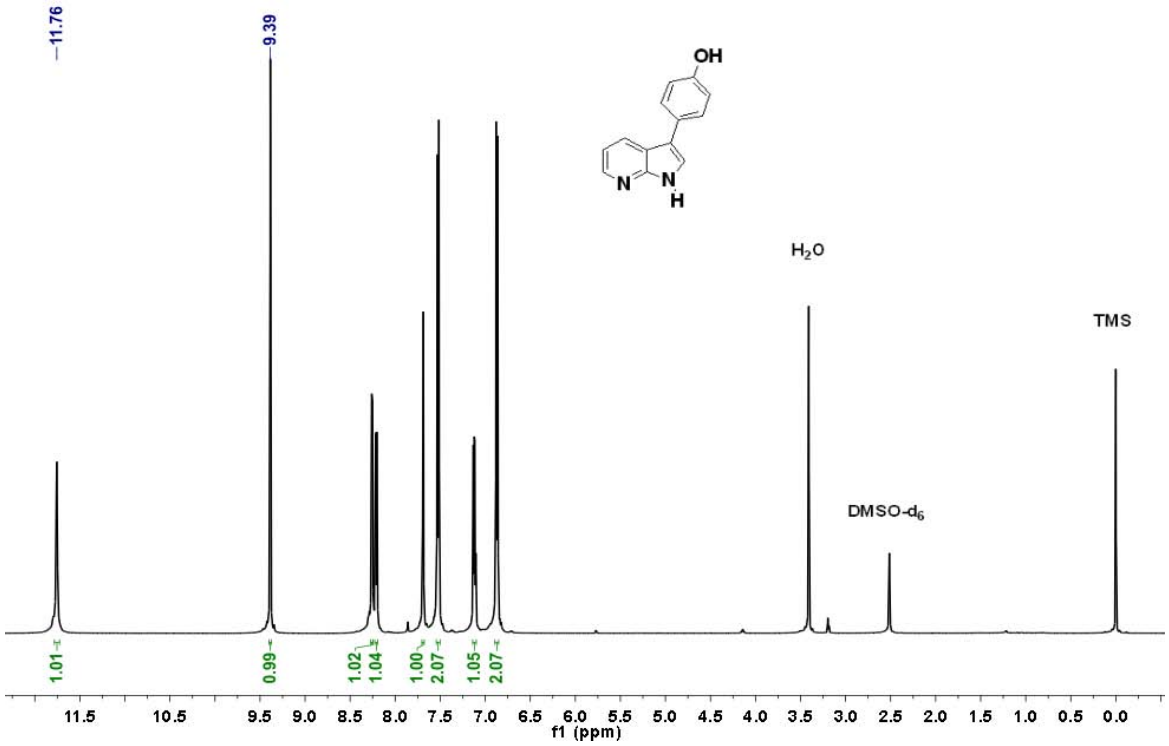
^{1}H NMR of **4g** (15 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm). *Impuruties from residual solvents.



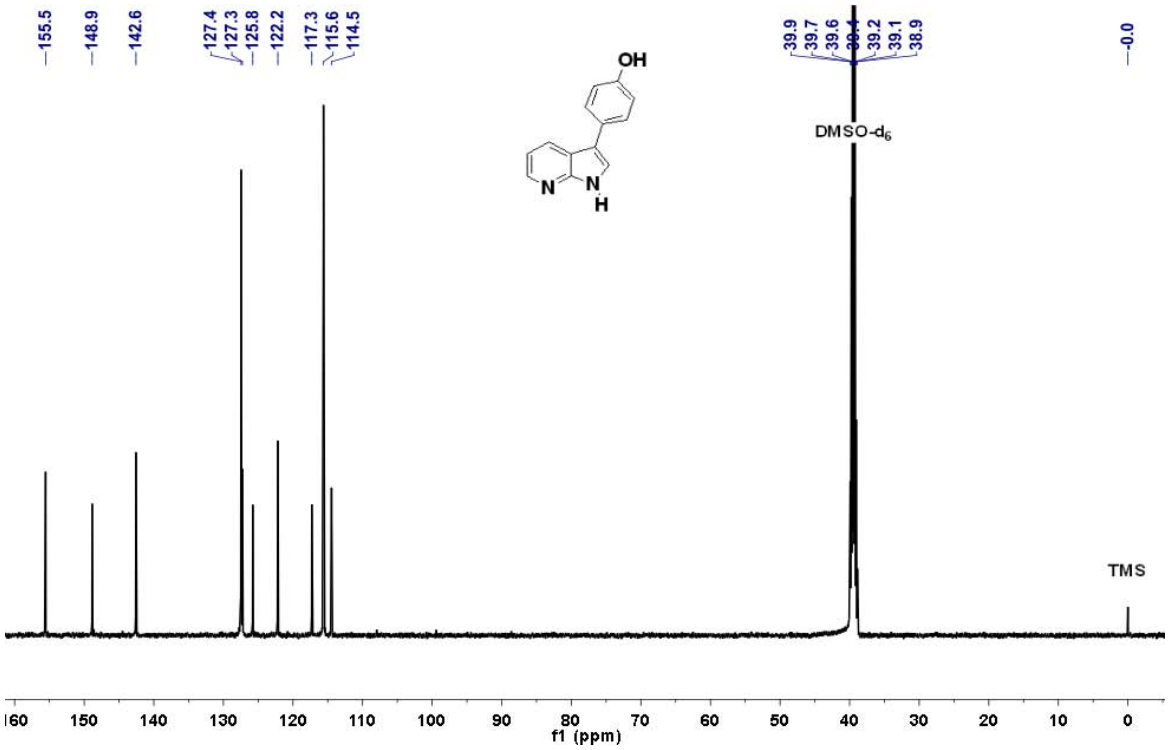
^{13}C NMR of **4g** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



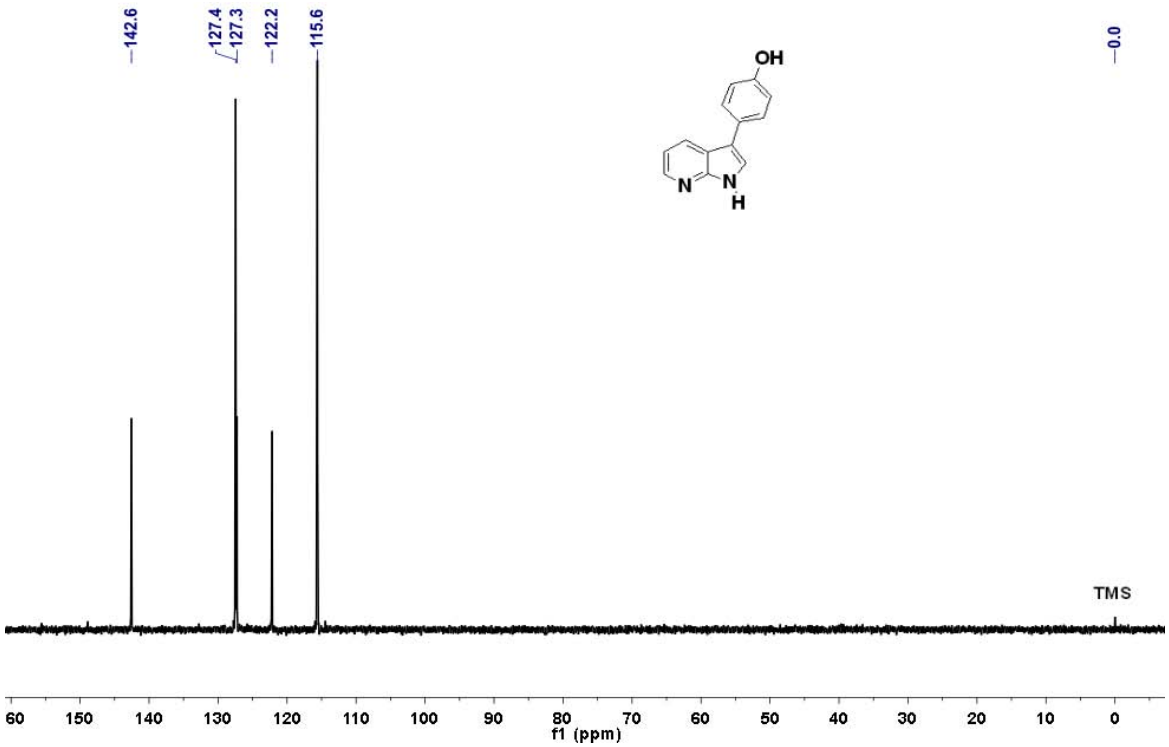
^{13}C DEPT 135-NMR of **4g** (15 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



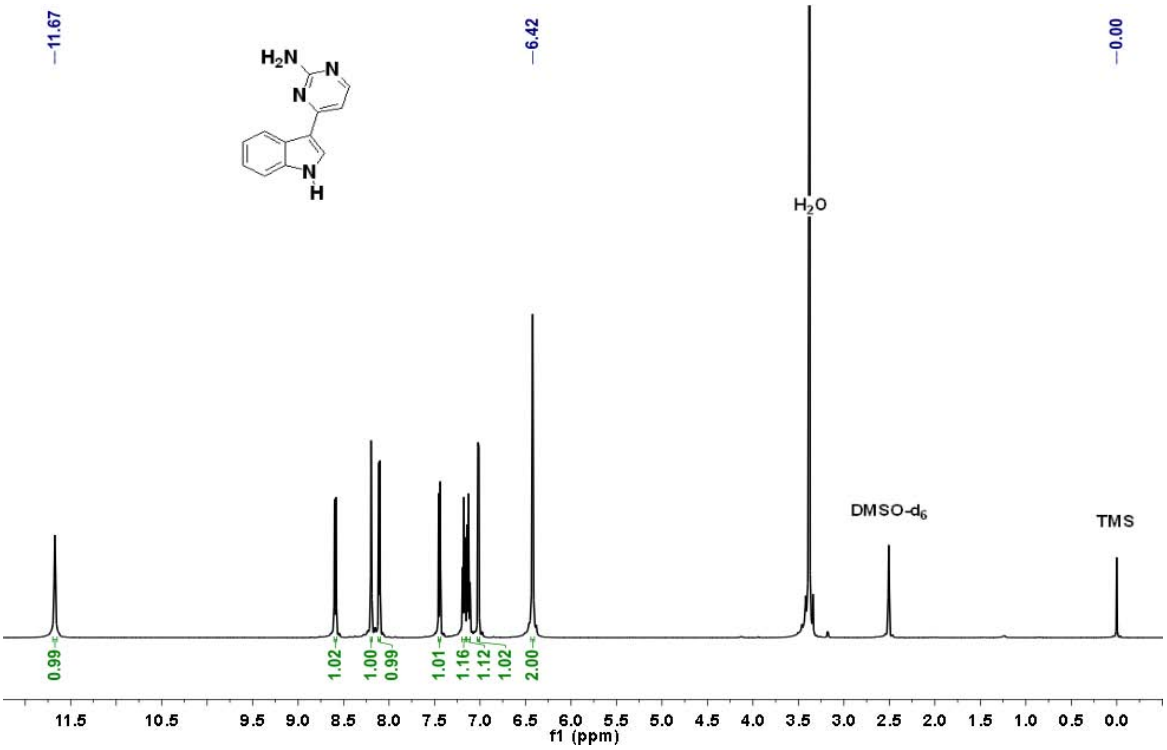
^{1}H NMR of **4h** (30 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



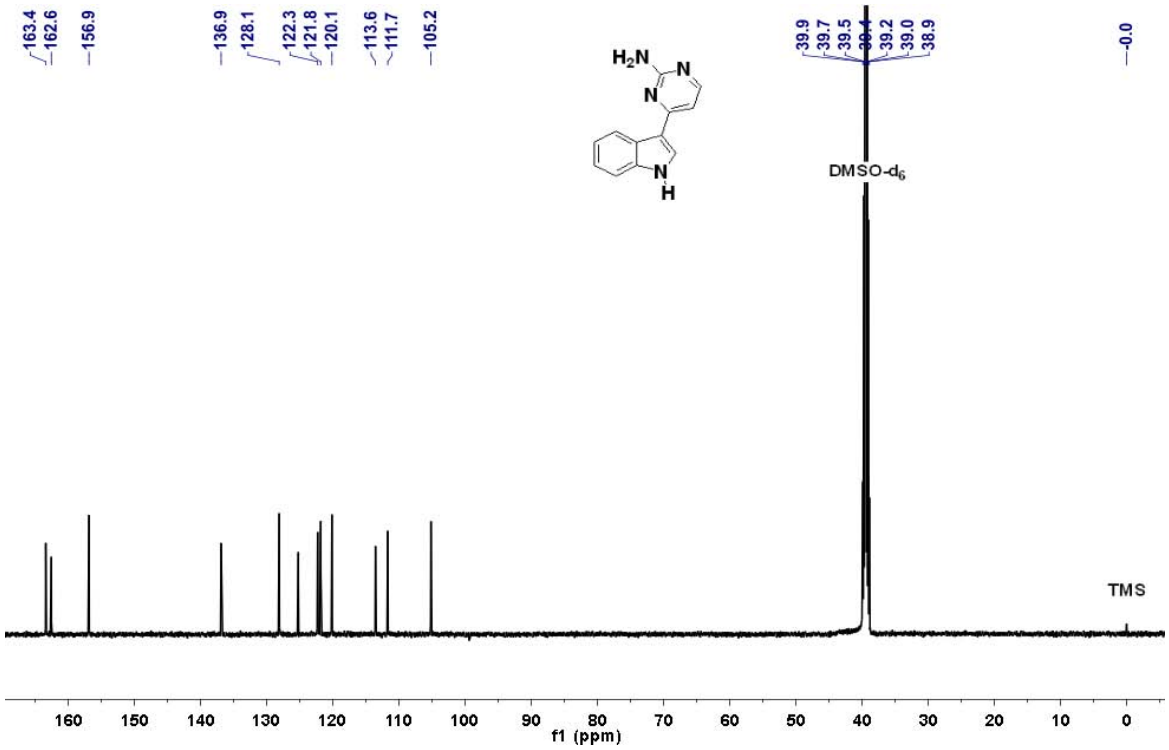
^{13}C NMR of **4h** (30 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



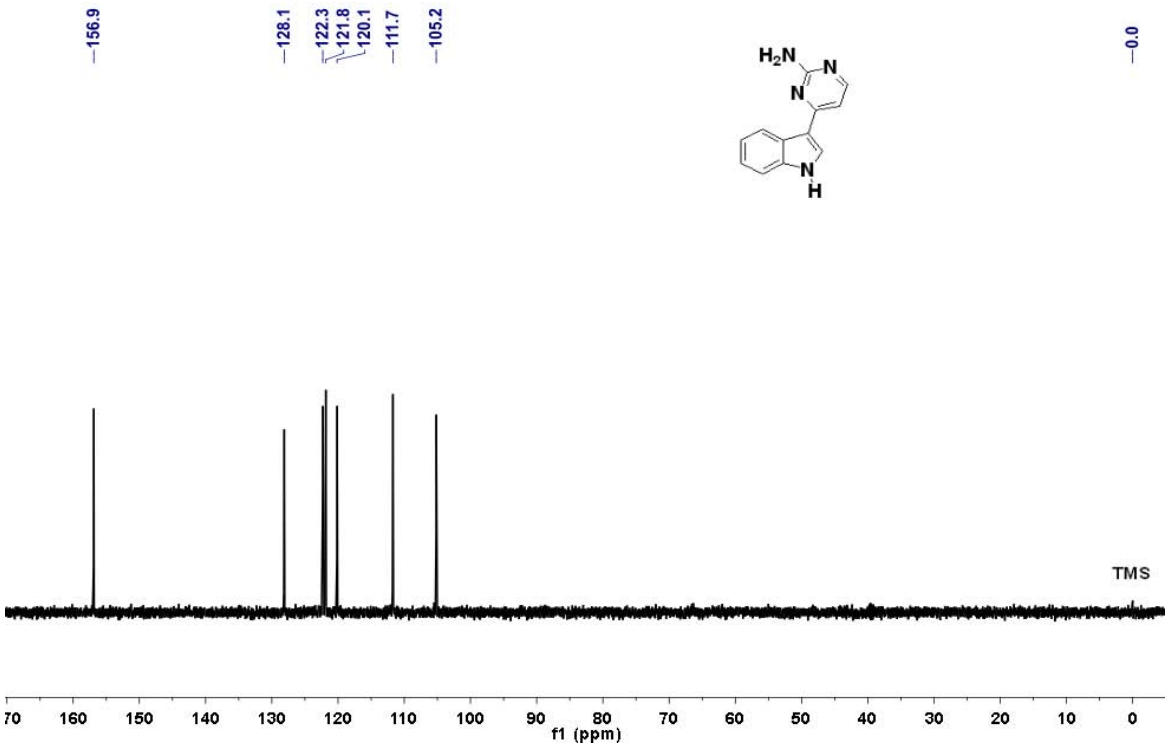
^{13}C DEPT 135-NMR of **4h** (30 mg) in 0.7 mL DMSO-d_6 at 295 K (δ in ppm).



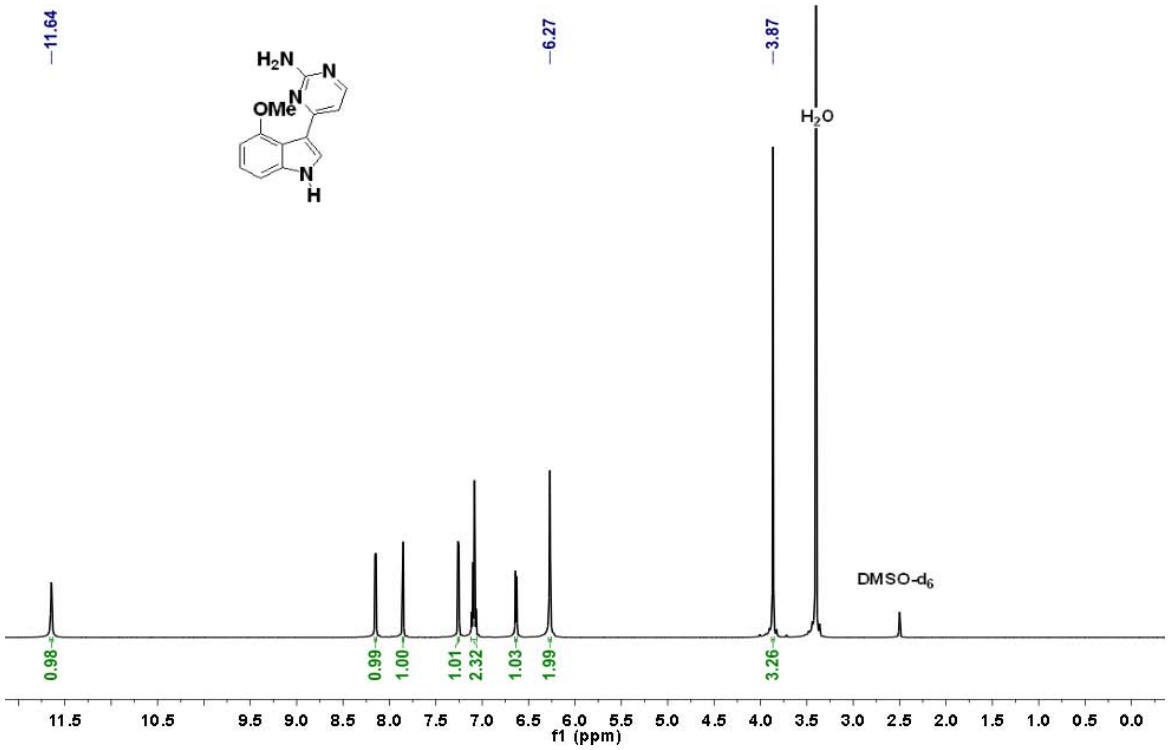
^{1}H NMR of **4i** (15 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



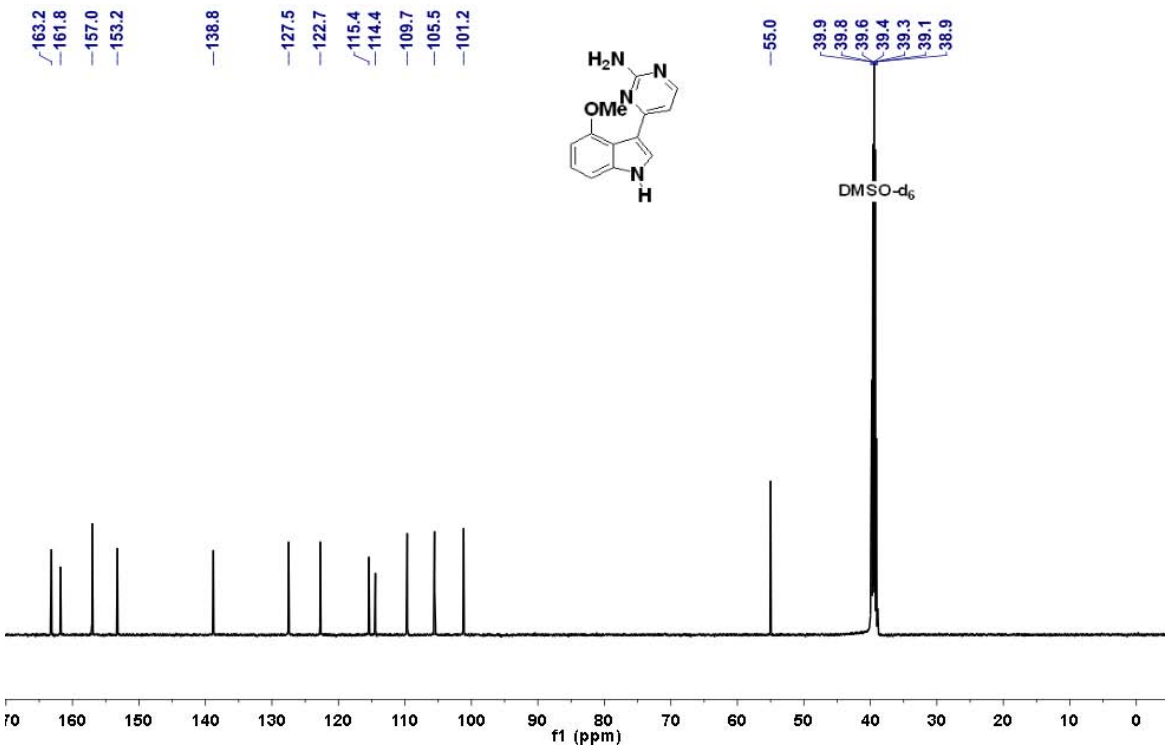
^{13}C NMR of **4i** (15 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



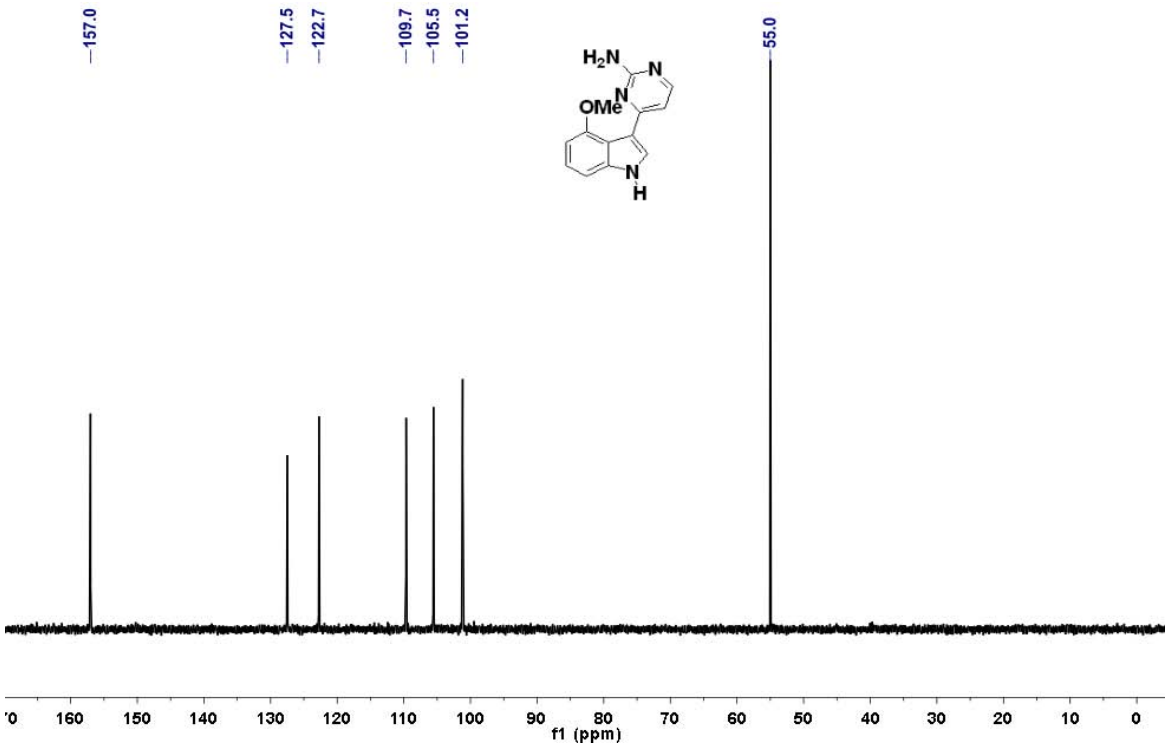
^{13}C DEPT 135-NMR of **4i** (15 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



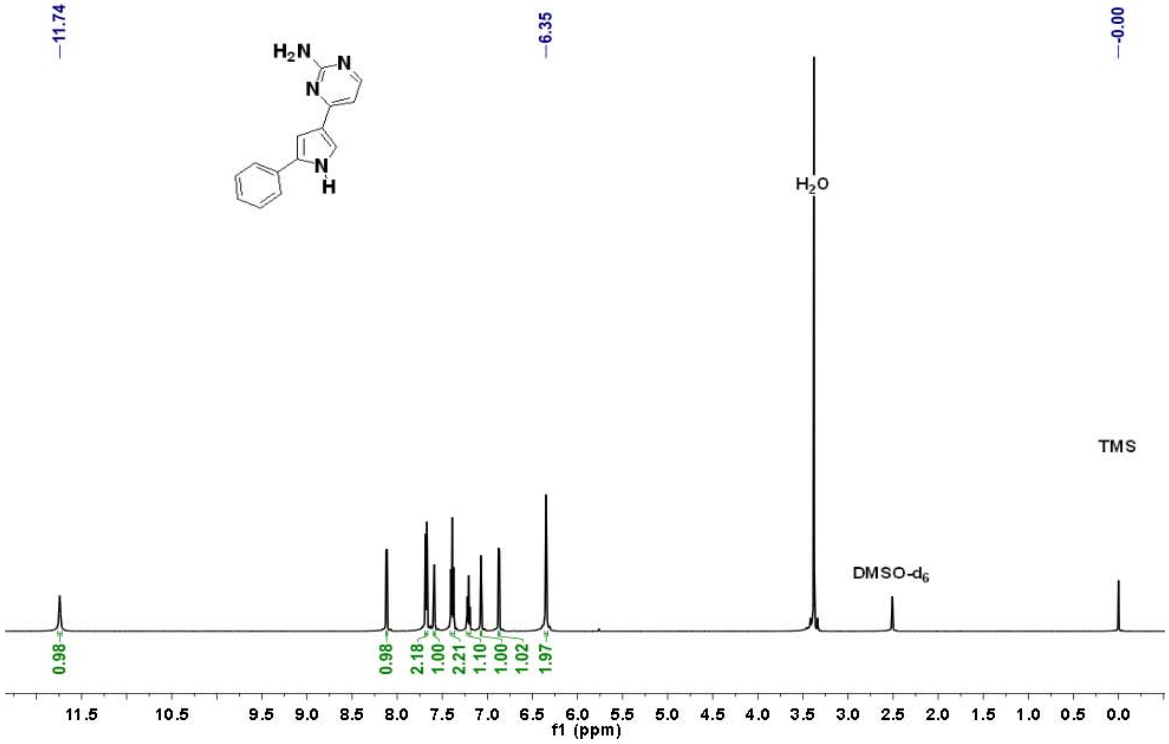
^{1}H NMR of **4j** (30 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



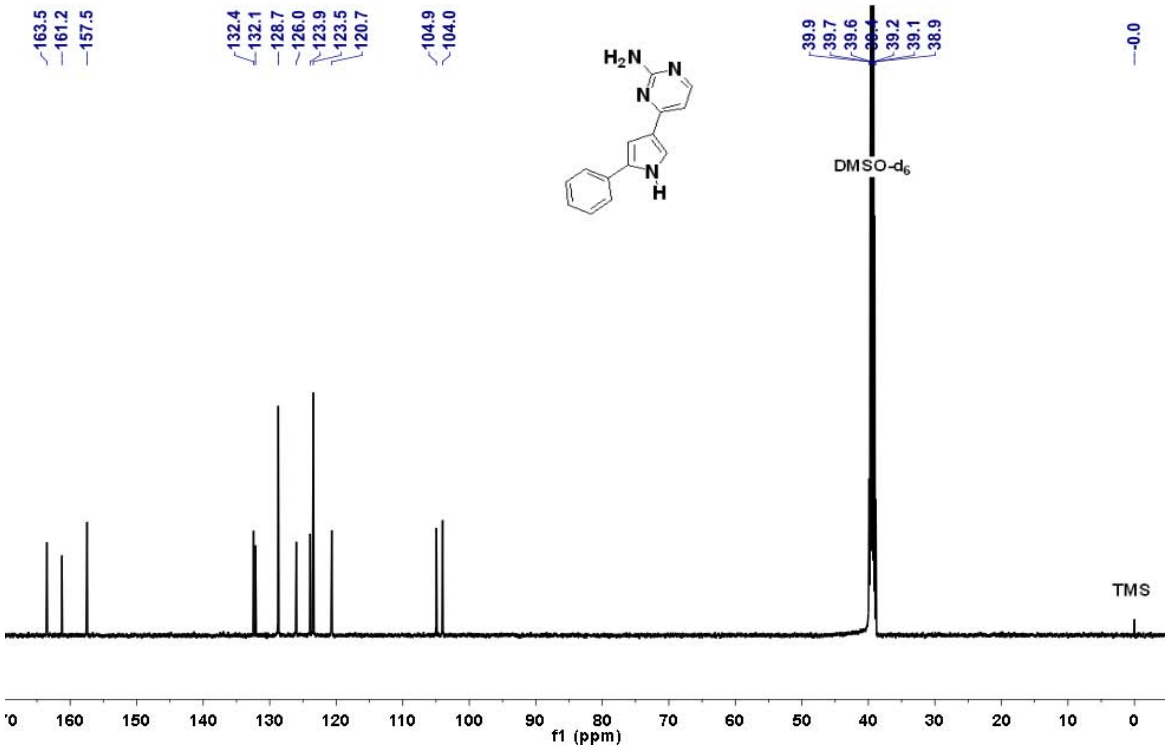
^{13}C NMR of **4j** (30 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



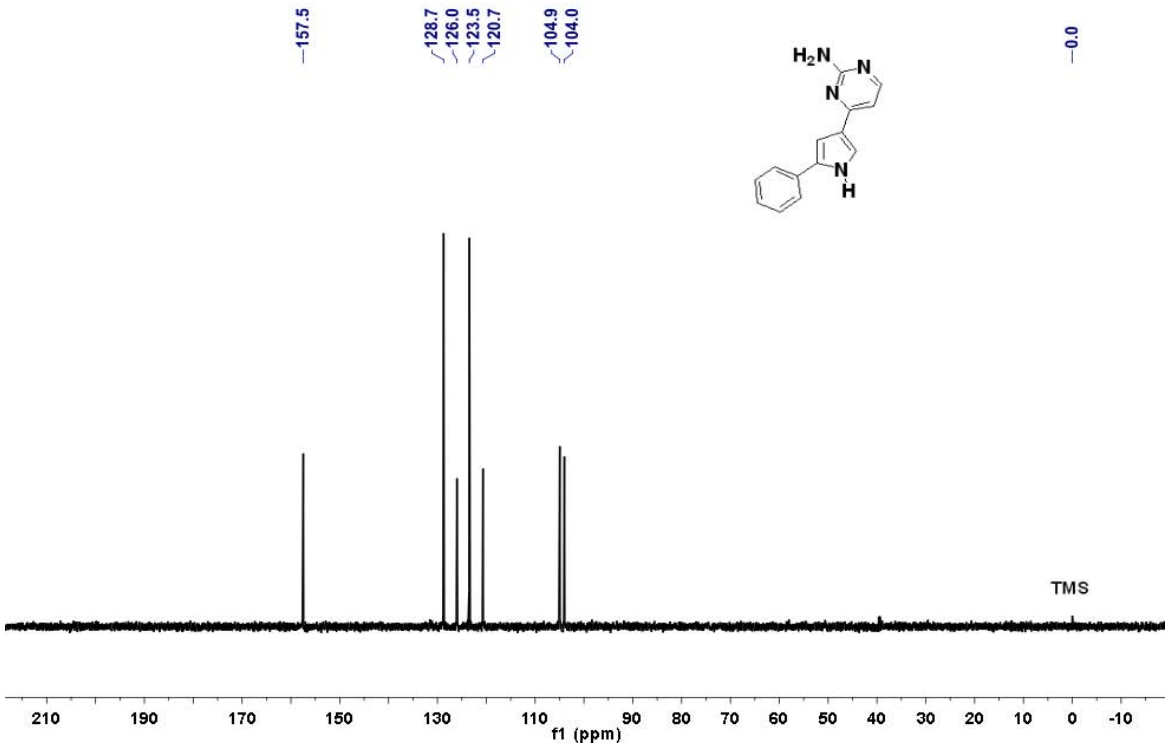
^{13}C DEPT 135-NMR of **4j** (30 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



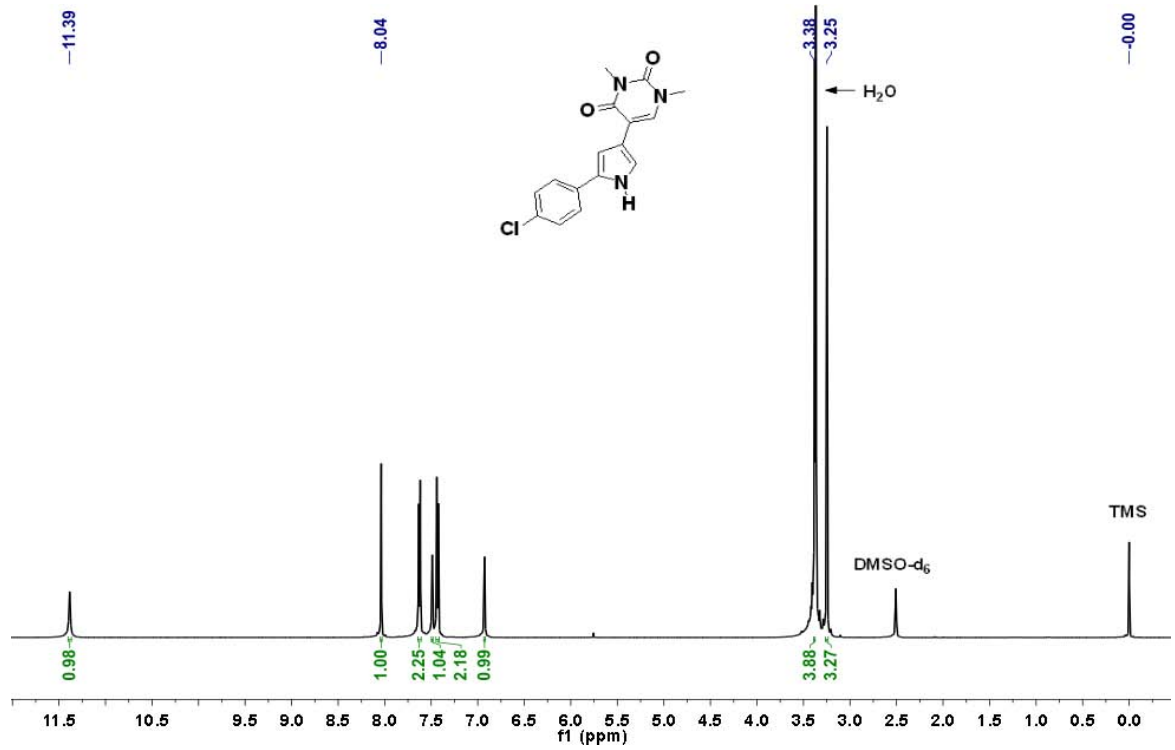
^{1}H NMR of **4k** (20 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



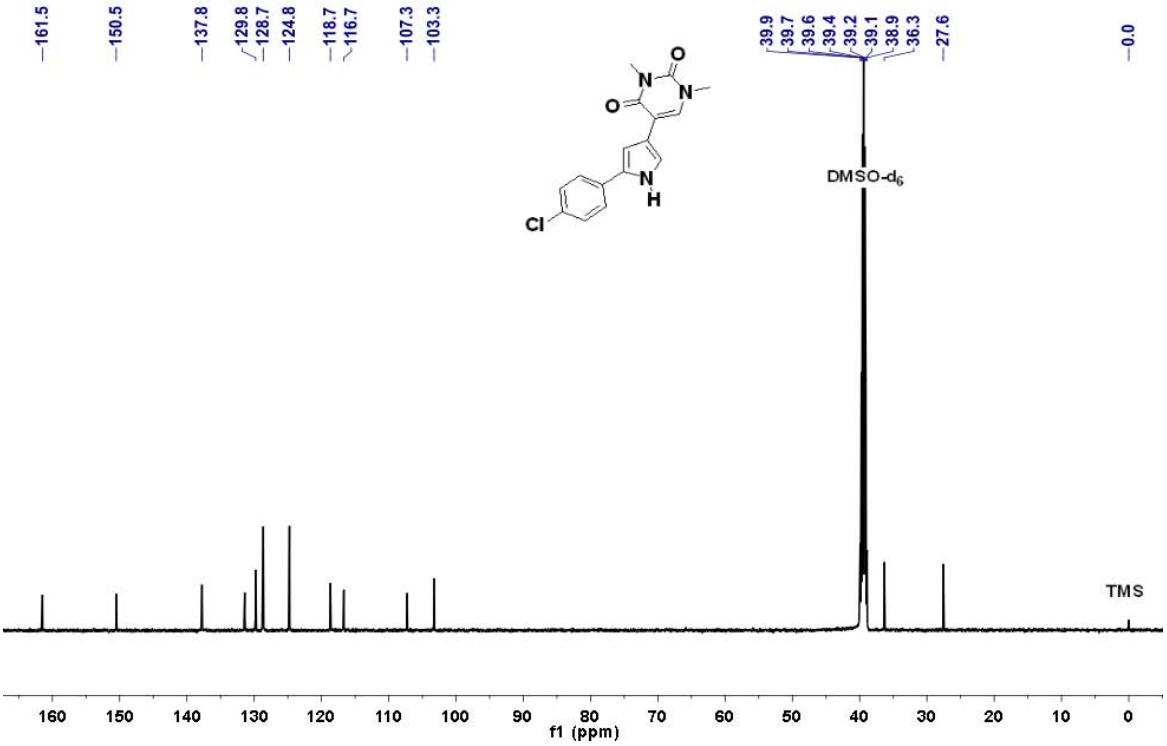
^{13}C NMR of **4k** (20 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



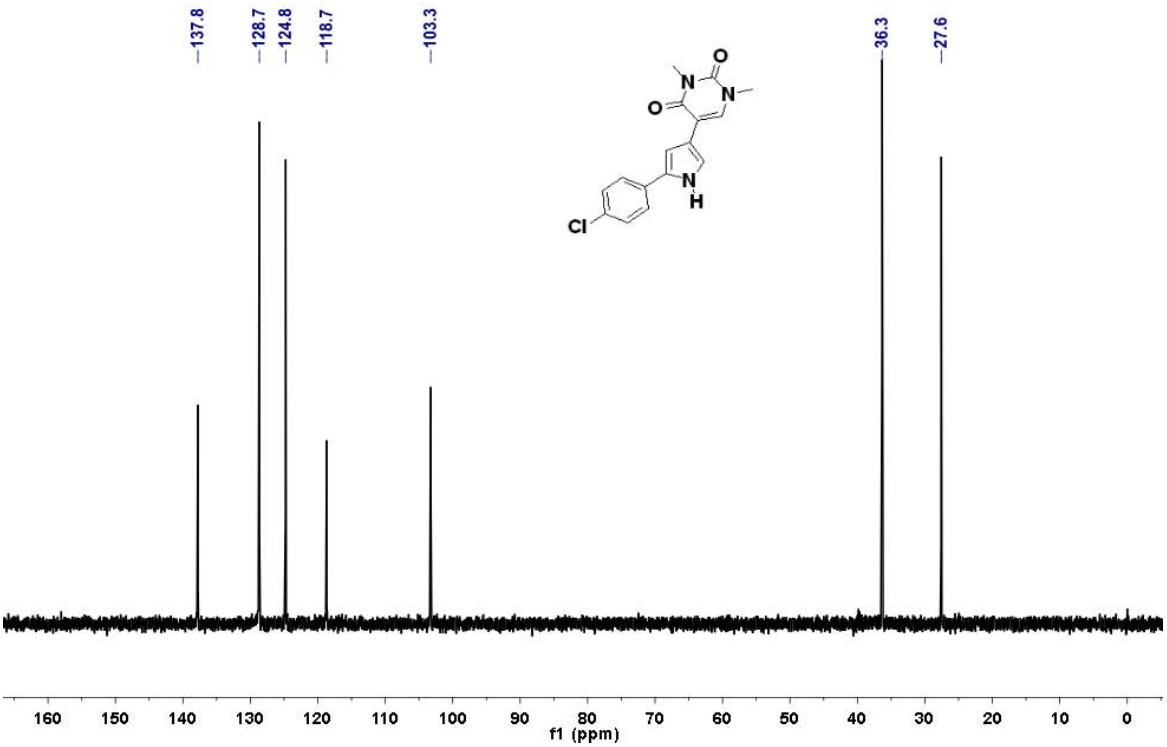
^{13}C DEPT 135-NMR of **4k** (20 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



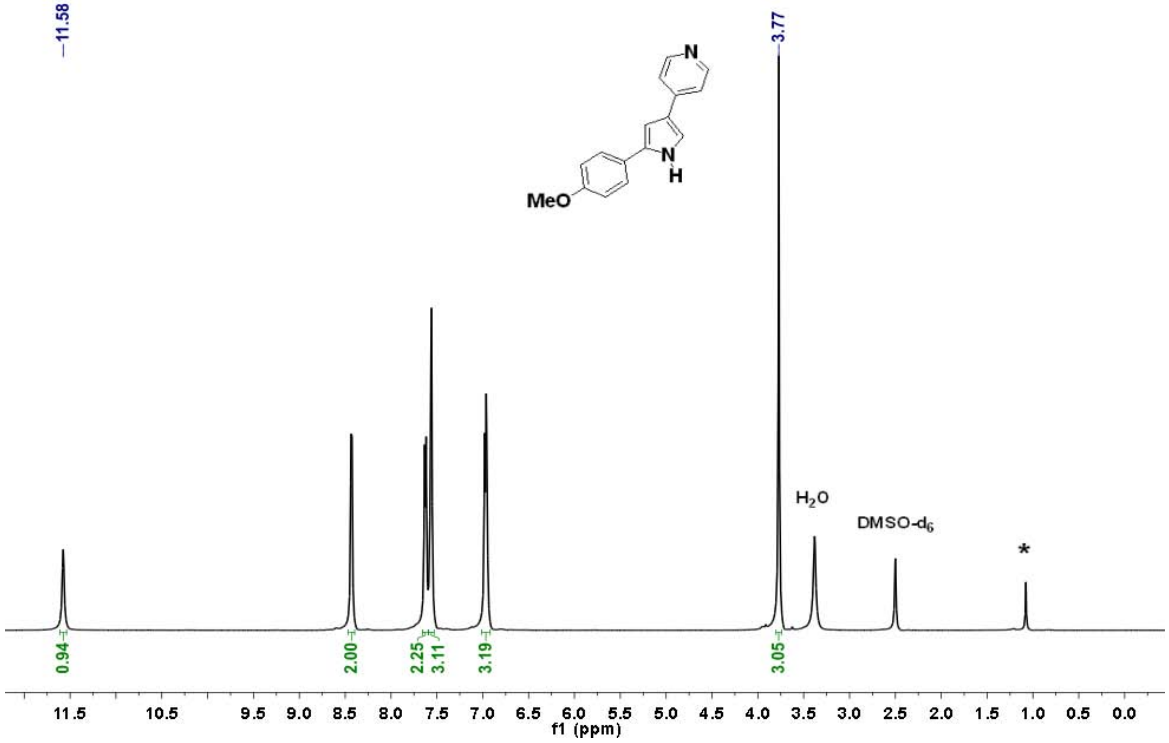
^{1}H NMR of **4l** (20 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



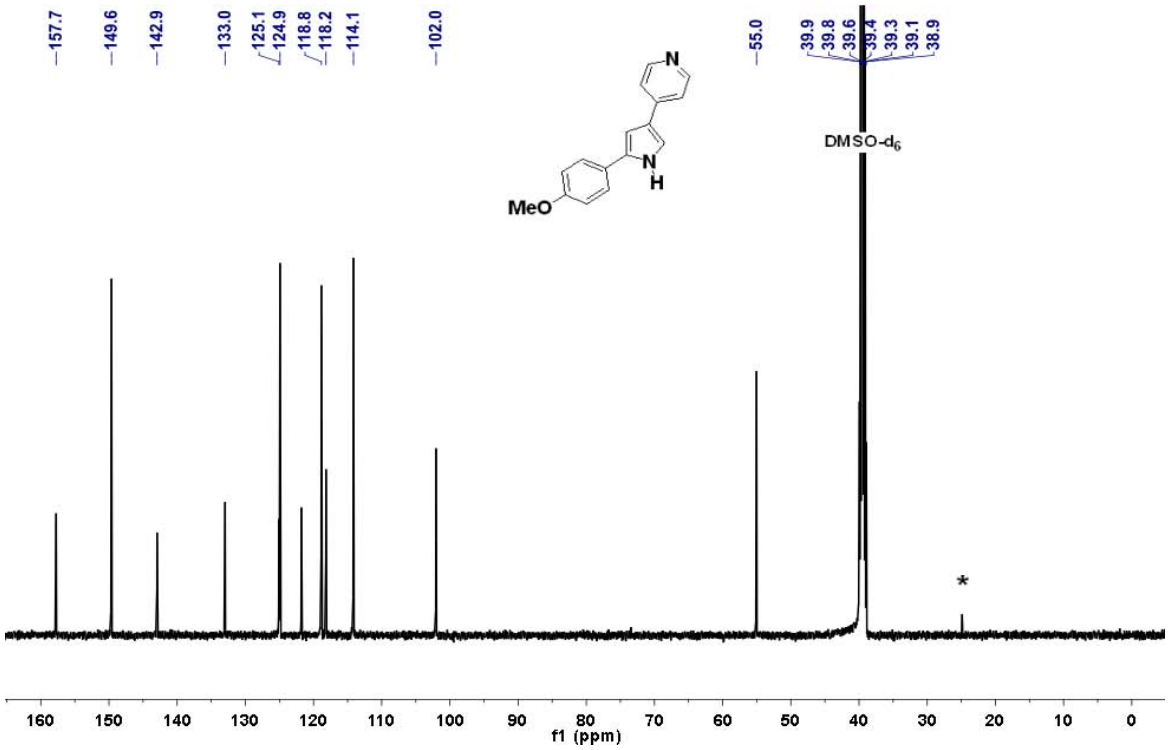
^{13}C NMR of **4l** (20 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



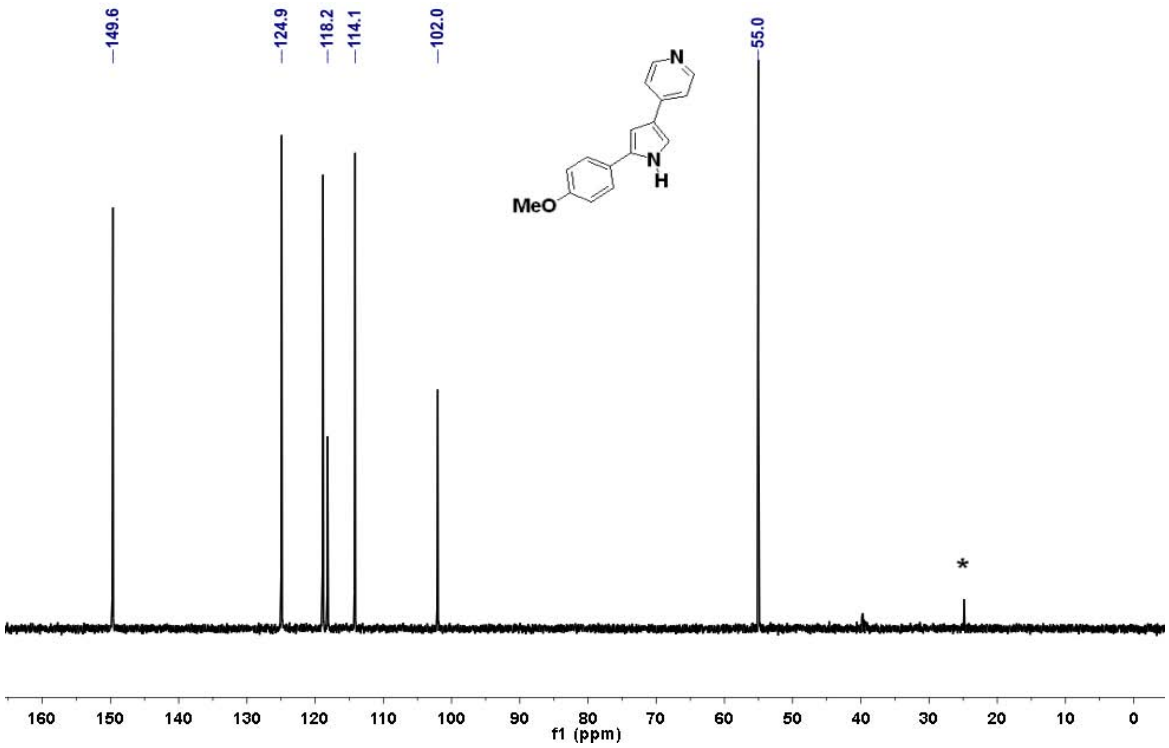
^{13}C DEPT 135-NMR of **4l** (20 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



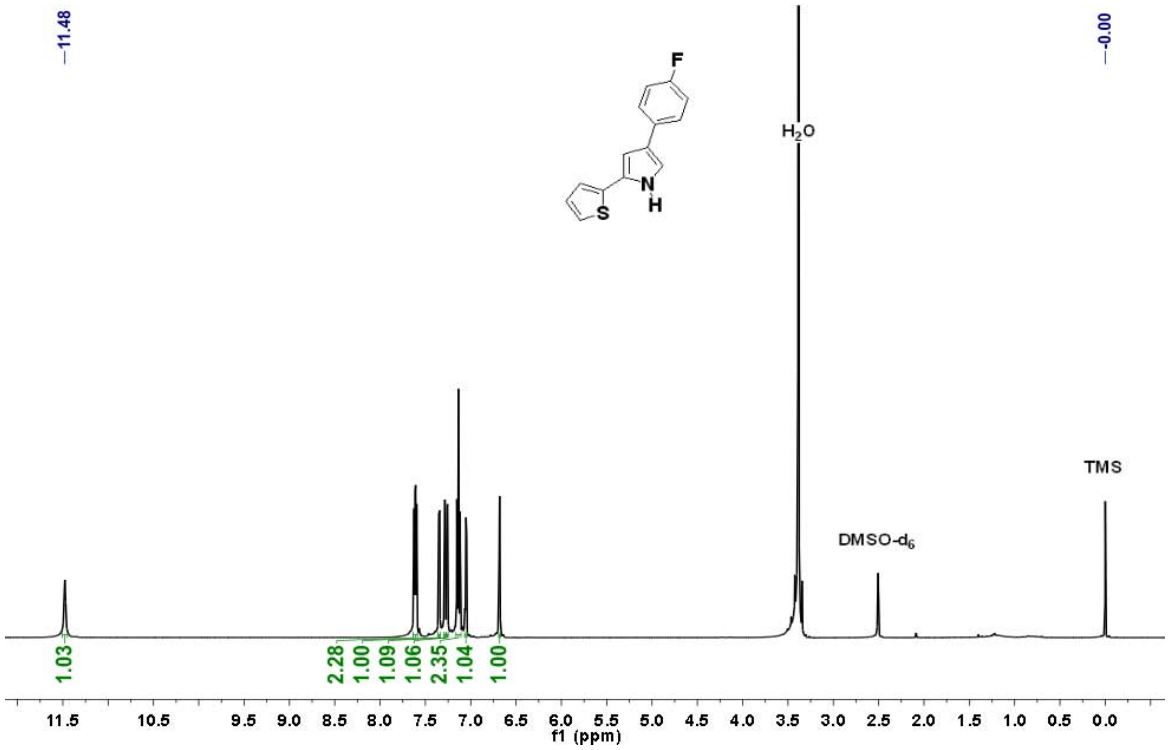
^{1}H NMR of **4m** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm). *Impurities from residual solvents.



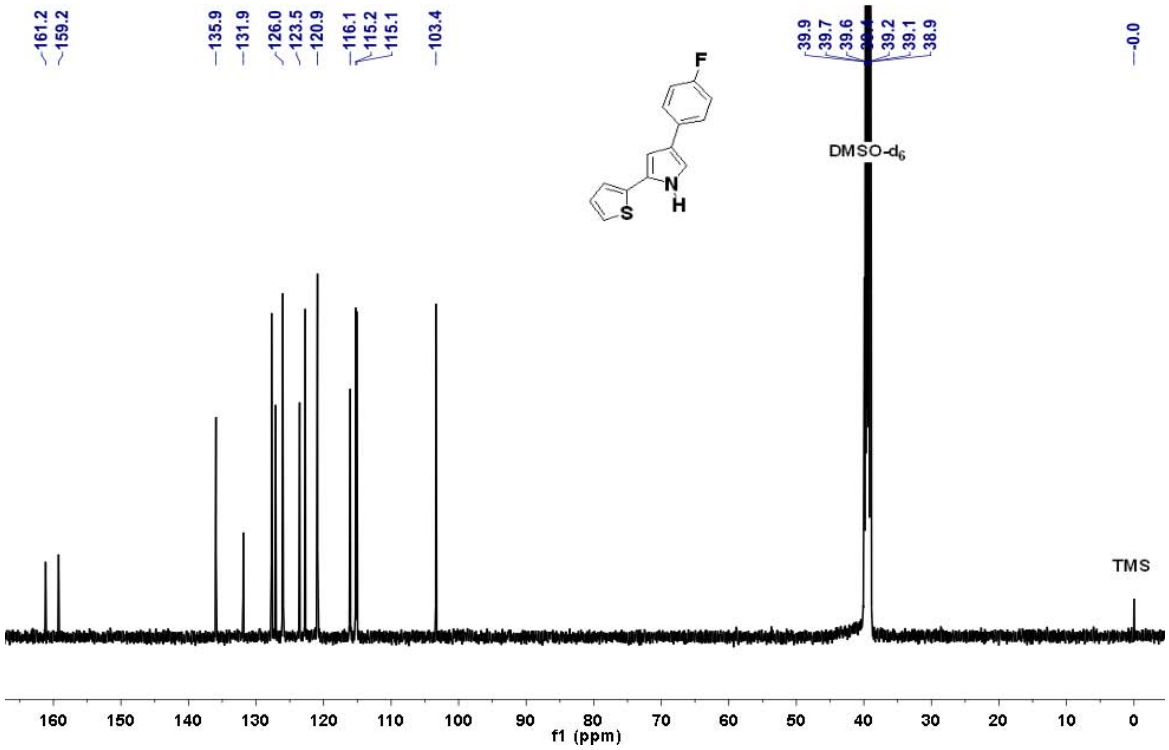
^{13}C NMR of **4m** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm). *Impurities from residual solvents.



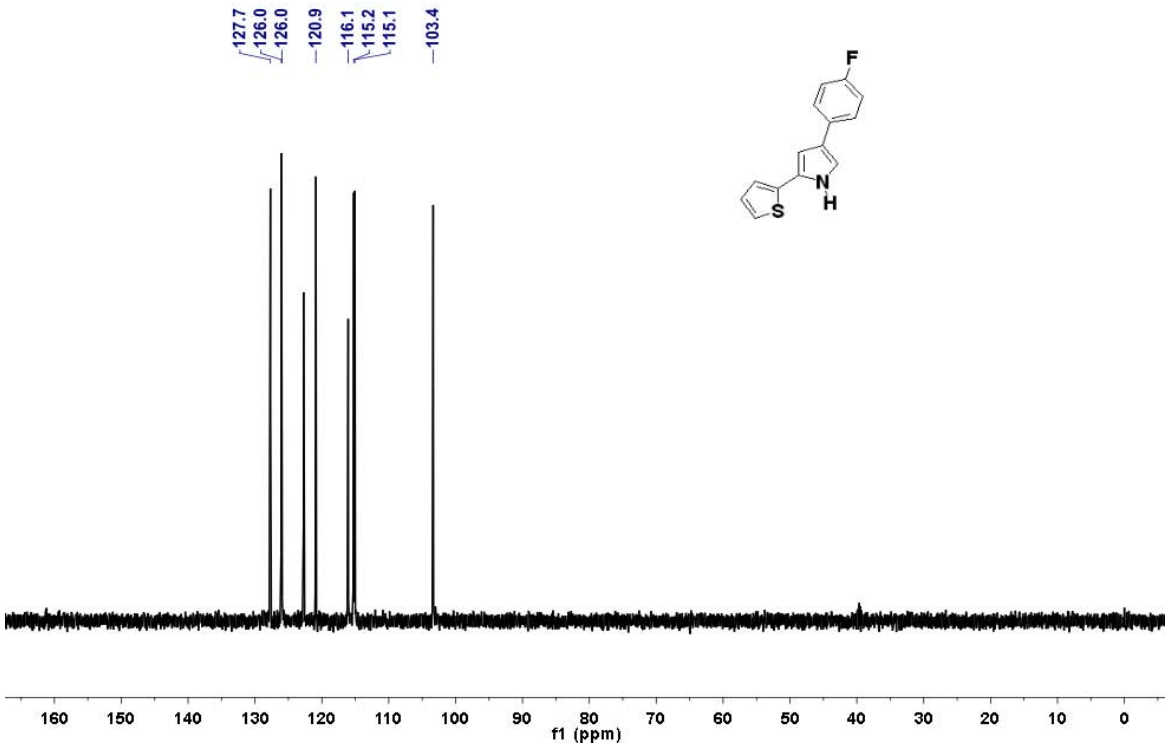
^{13}C DEPT 135-NMR of **4m** (15 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm). *Impurities from residual solvents.



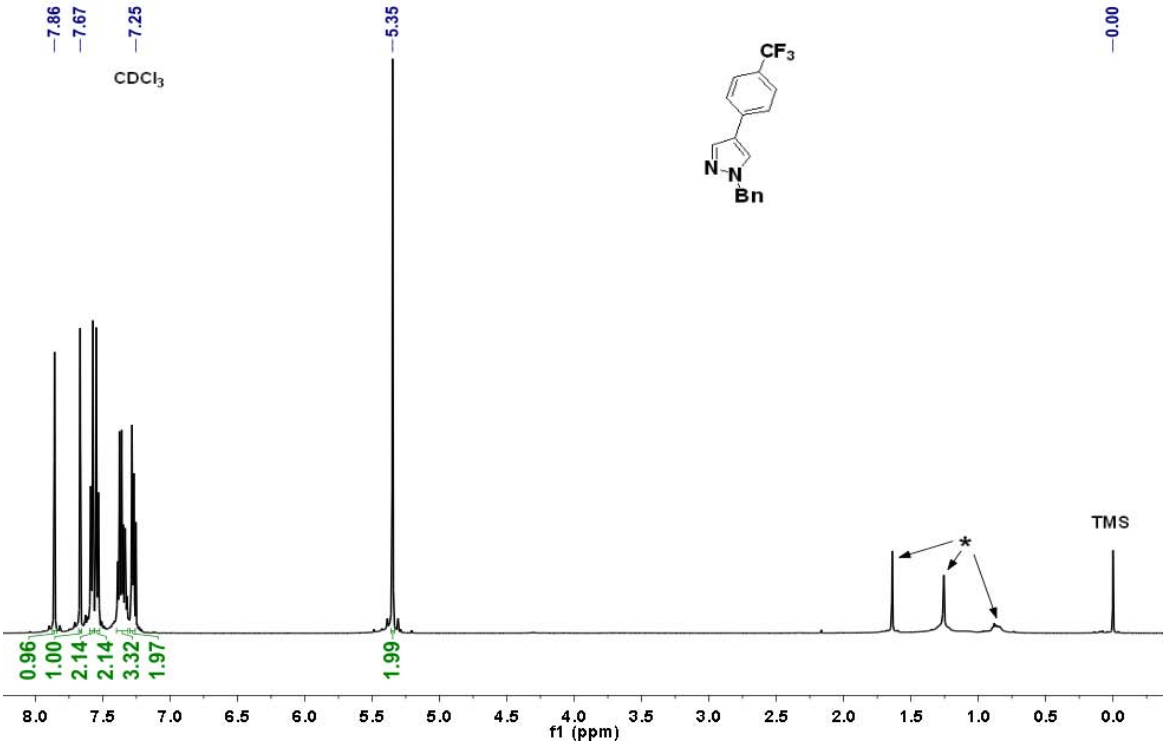
^{1}H NMR of **4n** (20 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



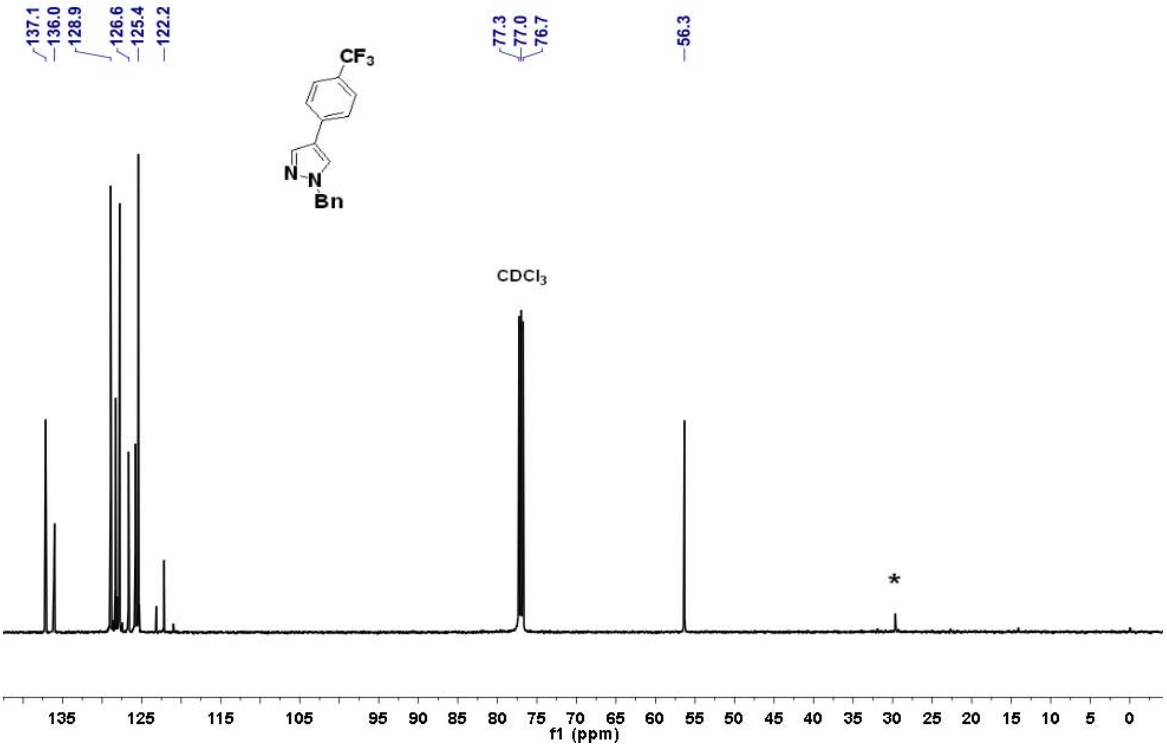
^{13}C NMR of **4n** (20 mg) in 0.7 mL DMSO-d_6 at 299 K (δ in ppm).



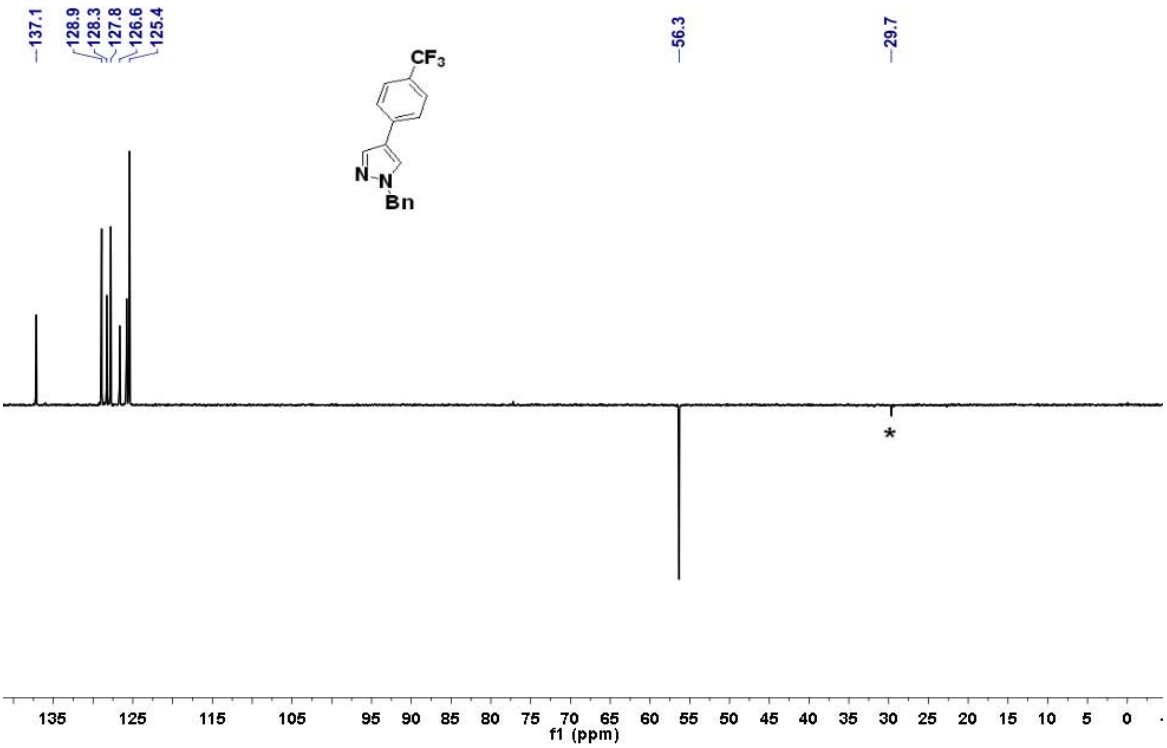
^{13}C DEPT 135-NMR of **4n** (20 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).



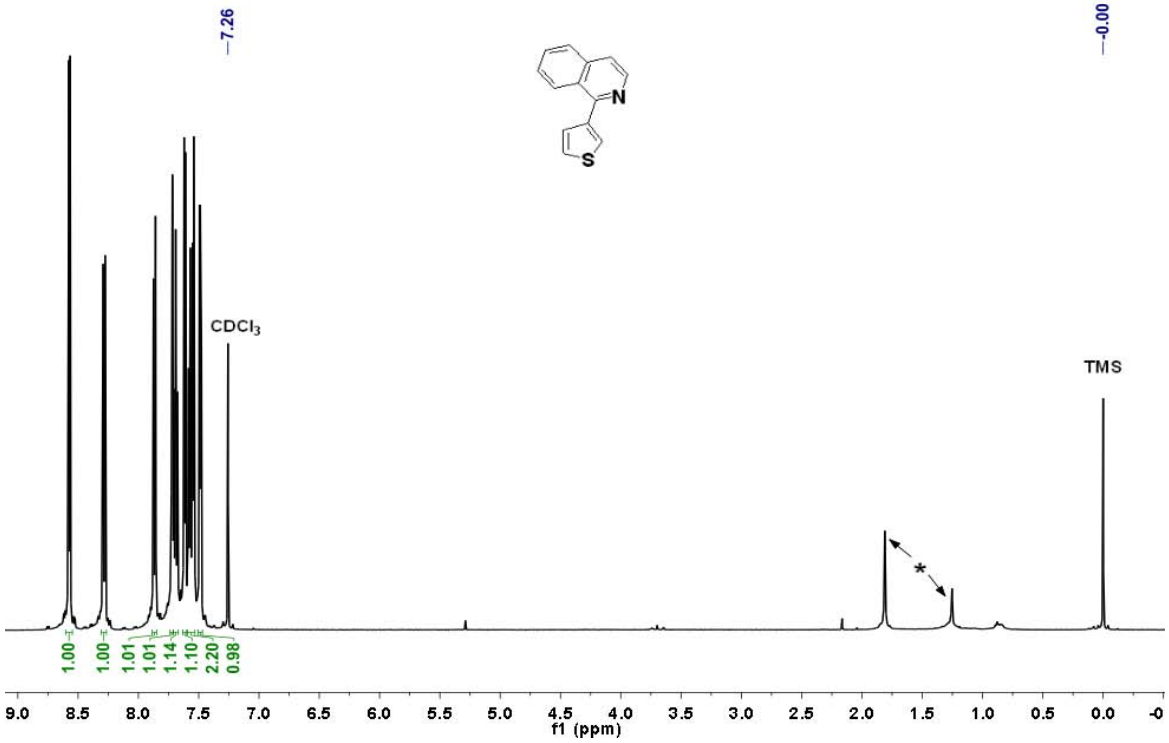
^{1}H NMR of **4o** (50 mg) in 0.7 mL $CDCl_3$ at 297 K (δ in ppm). *Impurities from residual solvents.



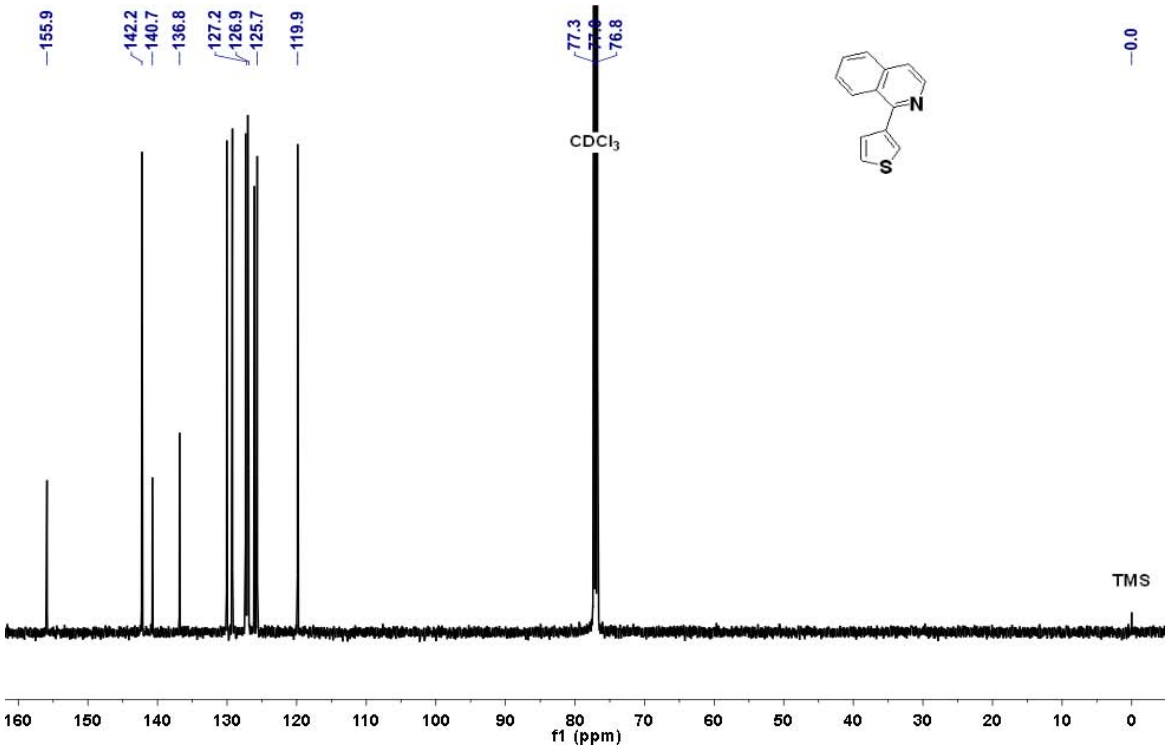
^{13}C NMR of **4o** (50 mg) in 0.7 mL $CDCl_3$ at 298 K (δ in ppm). *Impurities from residual solvents.



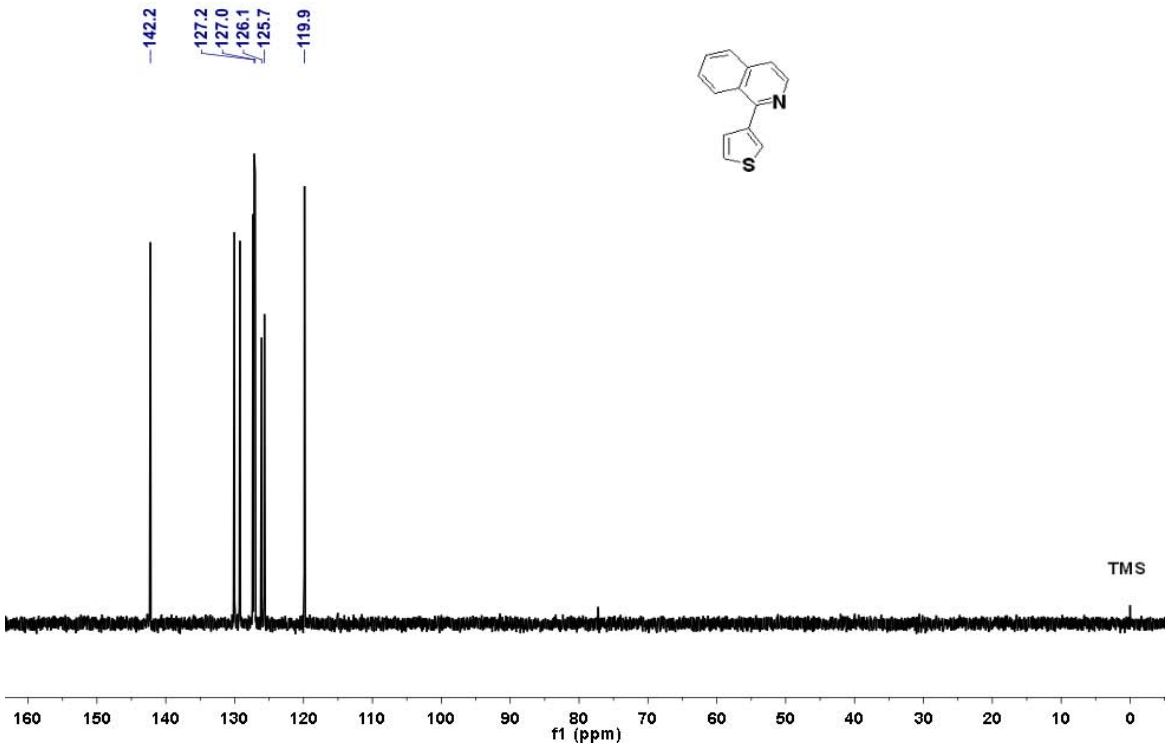
^{13}C DEPT 135-NMR of **4o** (50 mg) in 0.7 mL $CDCl_3$ at 297K (δ in ppm). *Impurities from residual solvents.



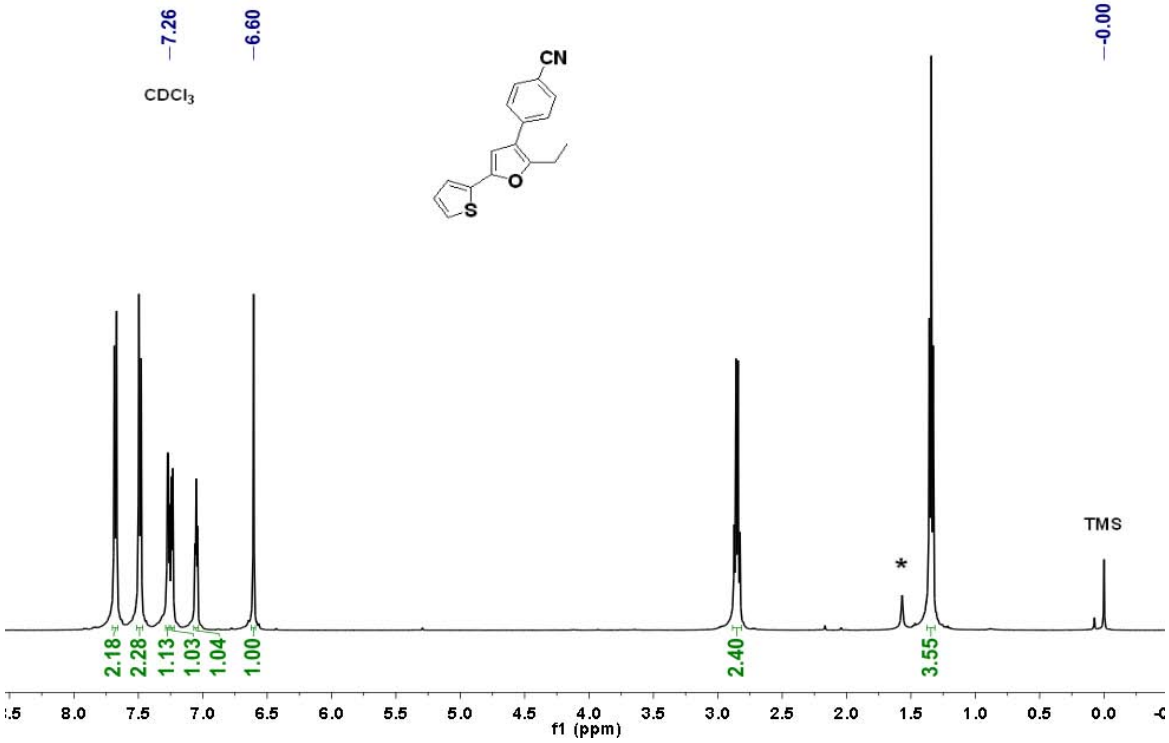
^{1}H NMR of **4p** (20 mg) in 0.7 mL $CDCl_3$ at 296 K (δ in ppm). *Impurities from residual solvents.



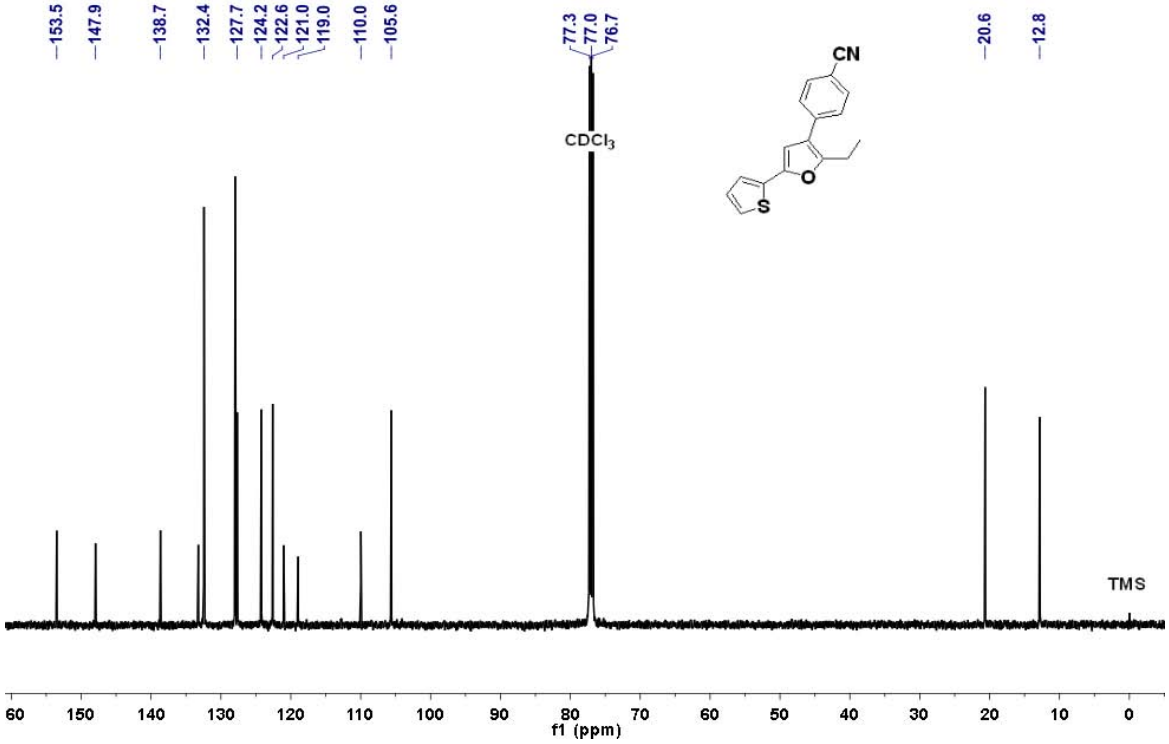
^{13}C NMR of **4p** (20 mg) in 0.7 mL $CDCl_3$ at 296 K (δ in ppm).



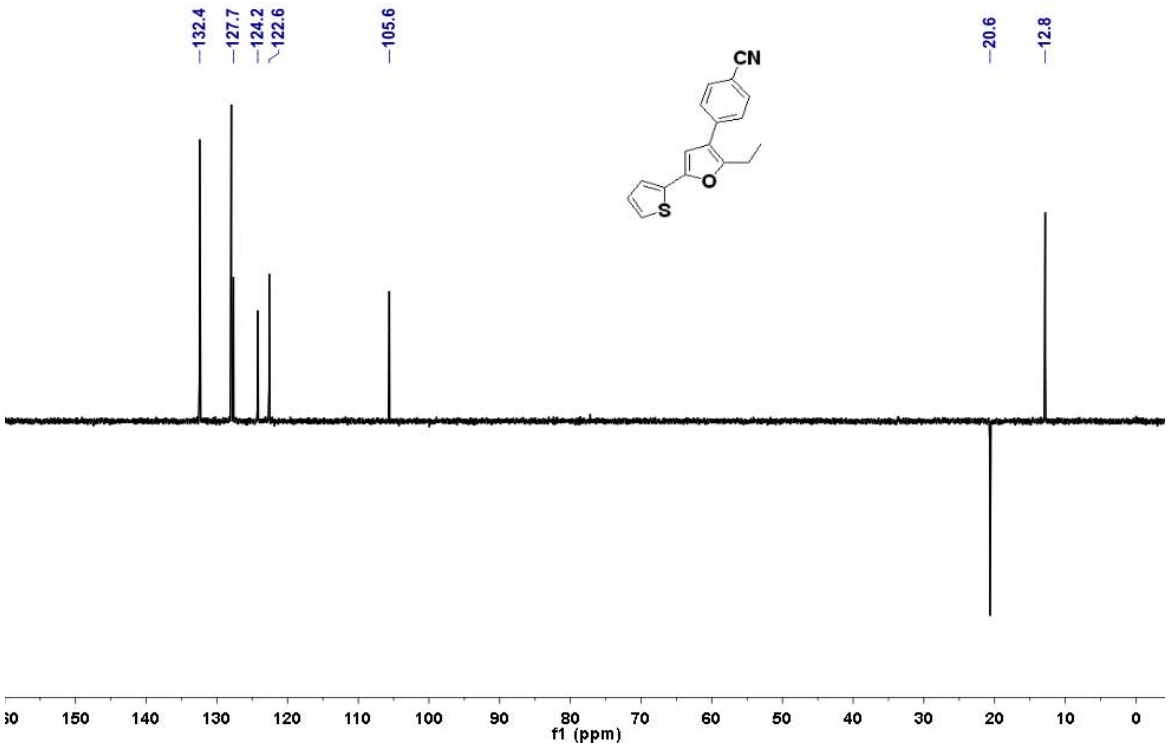
^{13}C DEPT 135-NMR of **4p** (20 mg) in 0.7 mL $CDCl_3$ at 296 K (δ in ppm).



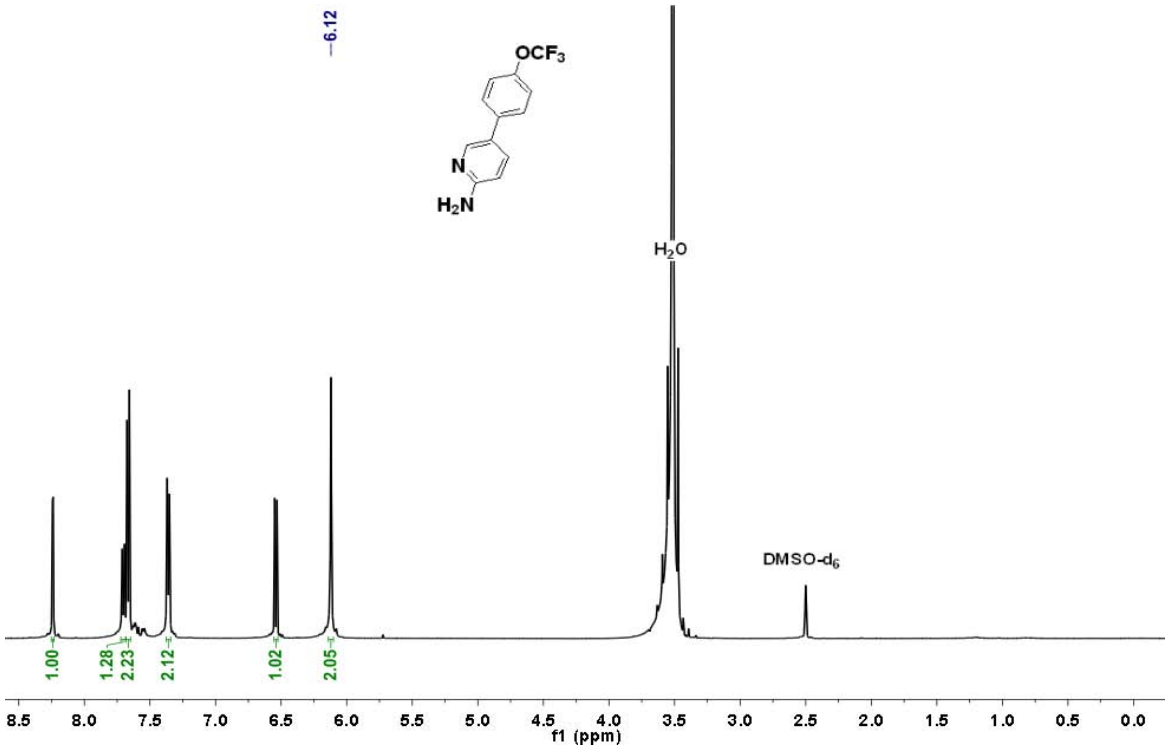
^{1}H NMR of **4q** (20 mg) in 0.7 mL $CDCl_3$ at 298 K (δ in ppm). *Impurities from residual solvents.



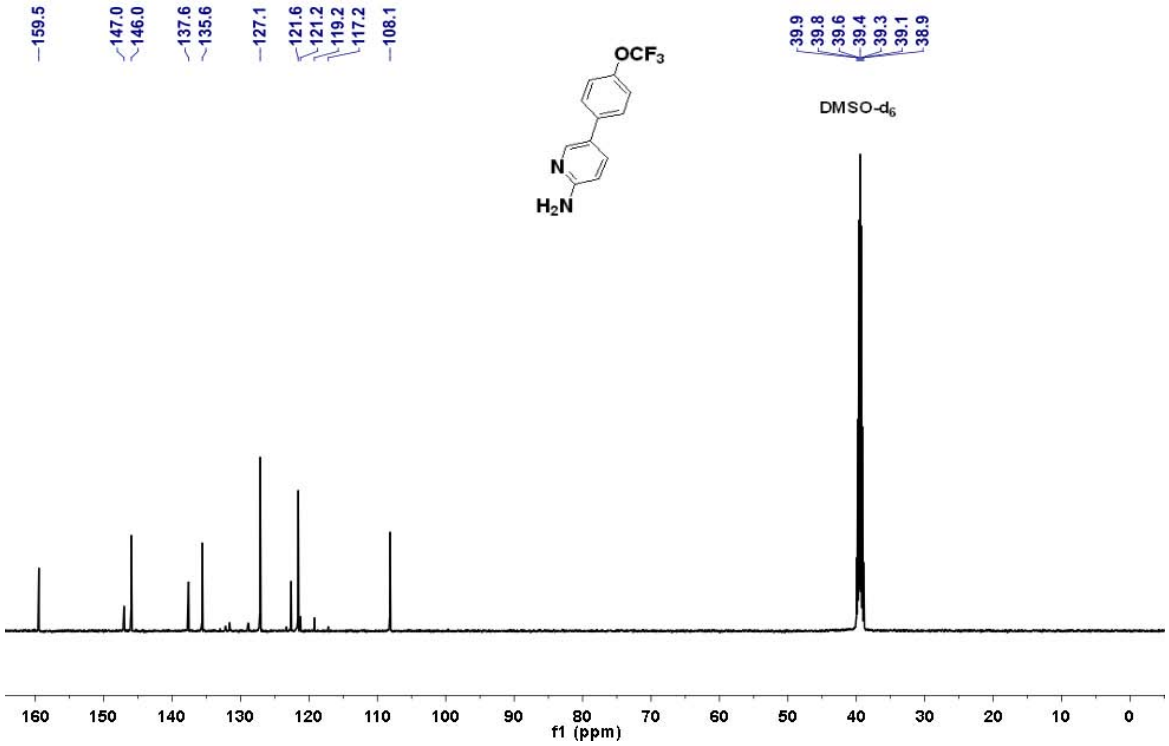
^{13}C NMR of **4q** (20 mg) in 0.7 mL $CDCl_3$ at 298 K (δ in ppm).



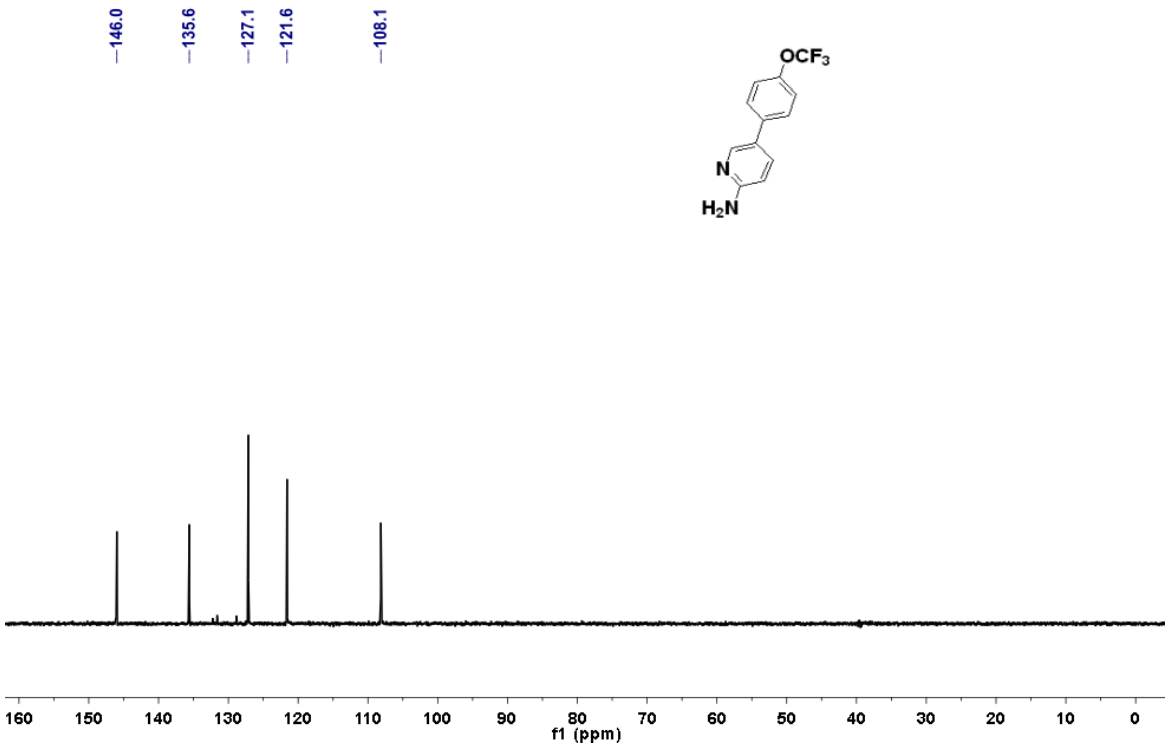
^{13}C DEPT 135-NMR of **4q** (20 mg) in 0.7 mL $CDCl_3$ at 298 K (δ in ppm).



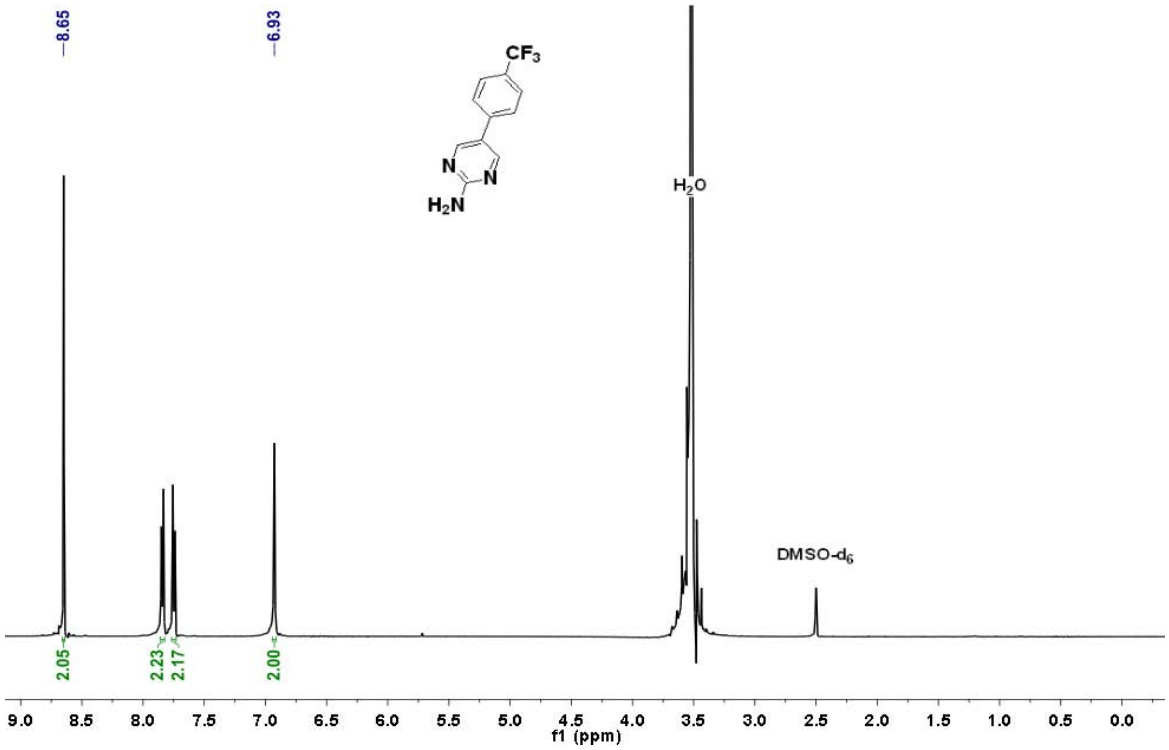
^{1}H NMR of **4r** (30 mg) in 0.7 mL $CDCl_3$ at 296 K (δ in ppm).



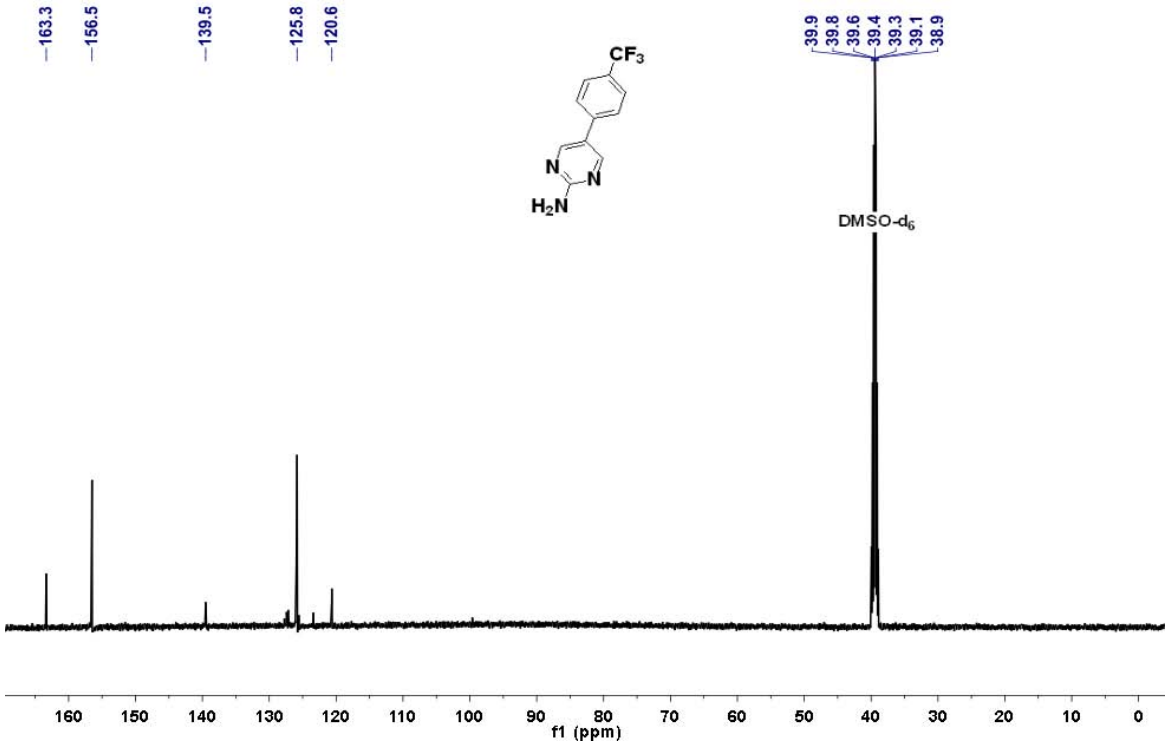
^{13}C NMR of **4r** (30 mg) in 0.7 mL $CDCl_3$ at 296 K (δ in ppm).



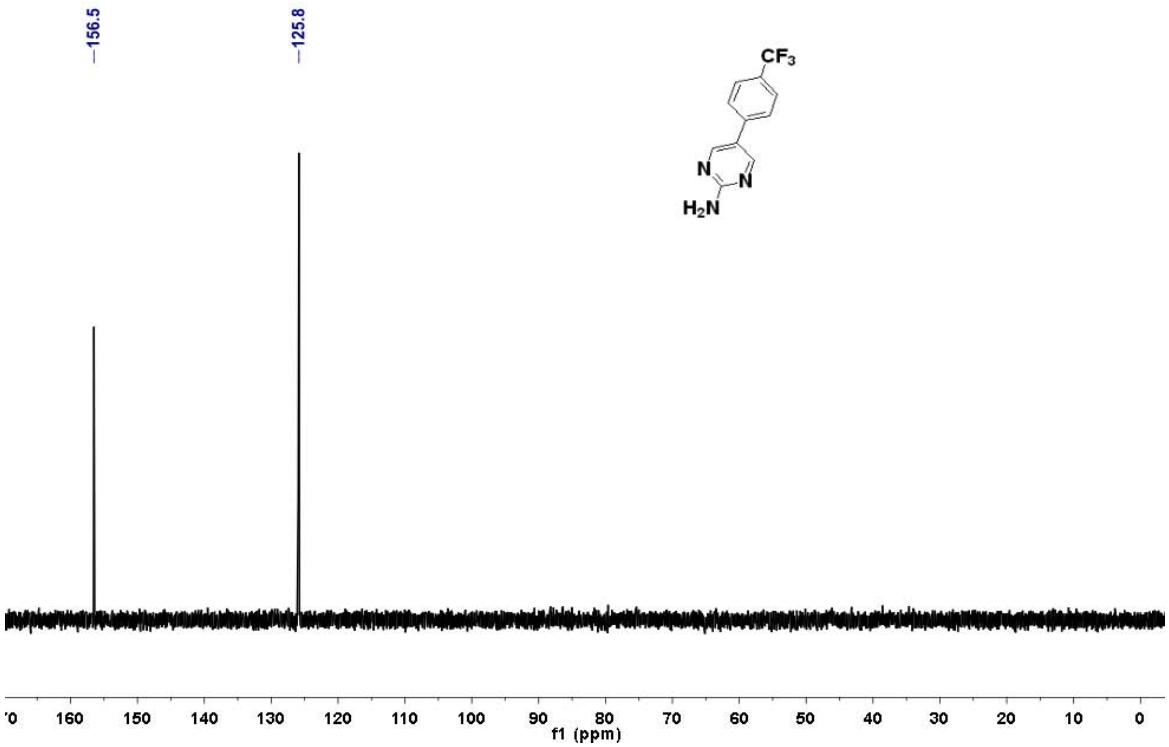
^{13}C DEPT 135-NMR of **4r** (30 mg) in 0.7 mL $CDCl_3$ at 296 K (δ in ppm).



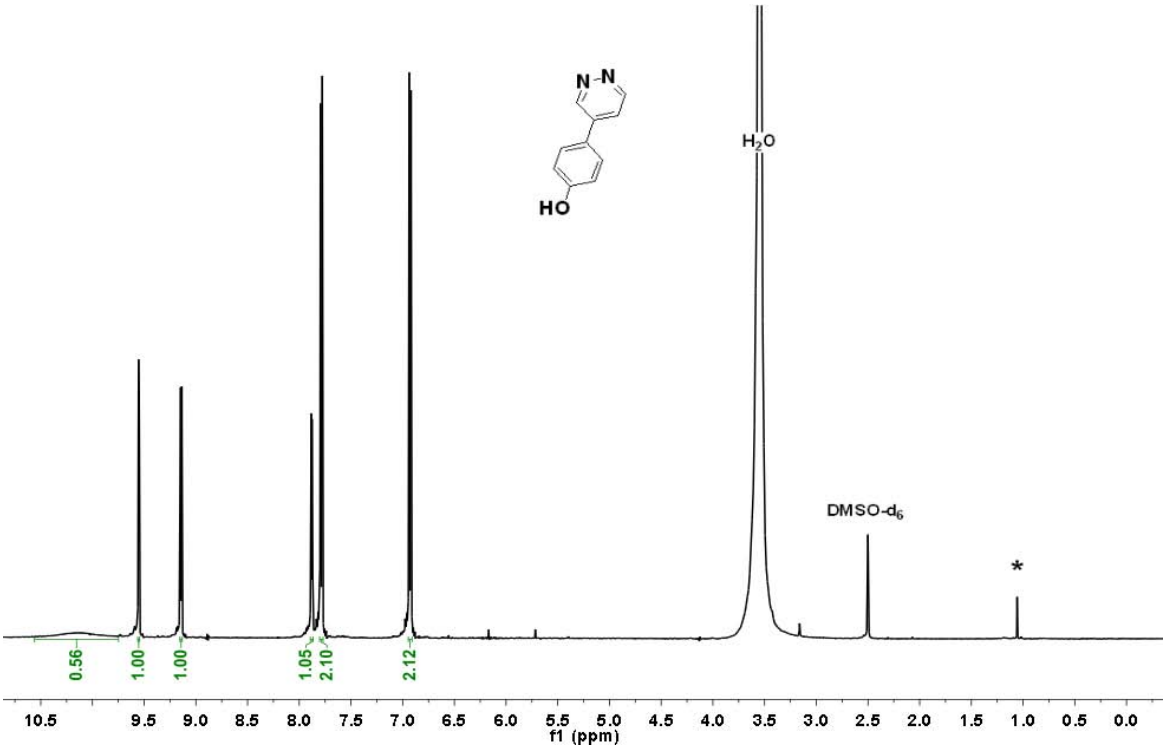
^{1}H NMR of **4s** (15 mg) in 0.7 mL $CDCl_3$ at 297 K (δ in ppm).



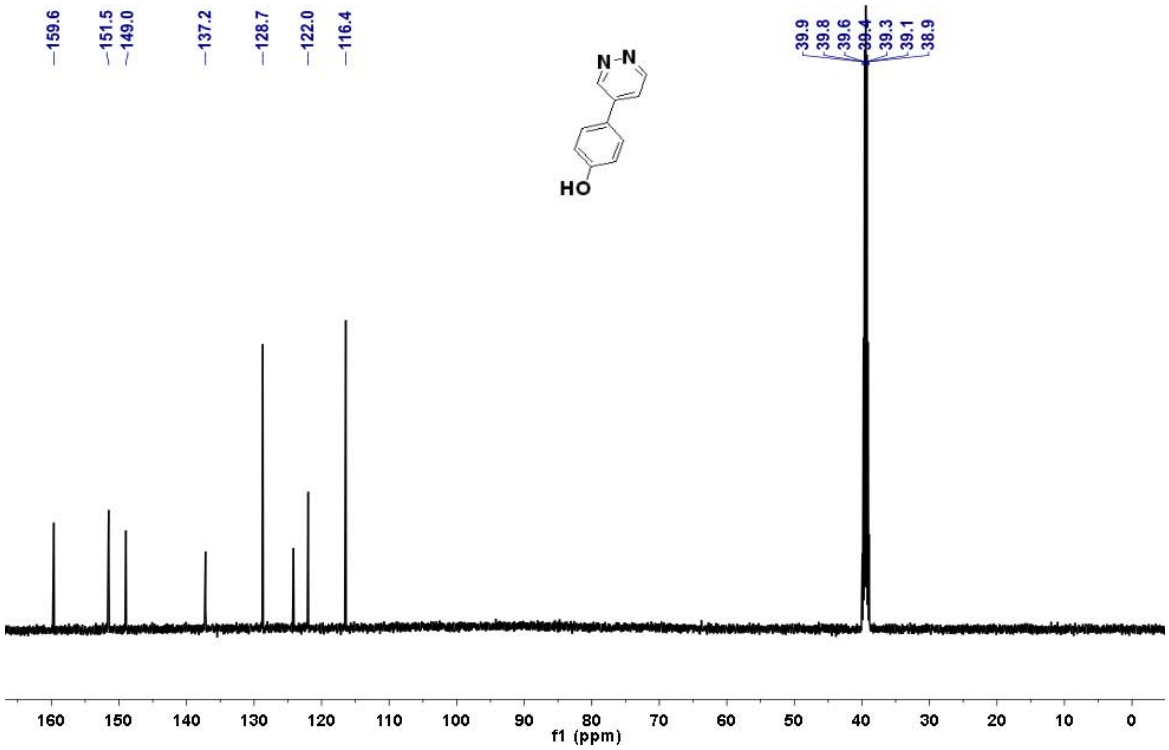
^{13}C NMR of **4s** (15 mg) in 0.7 mL $CDCl_3$ at 297 K (δ in ppm).



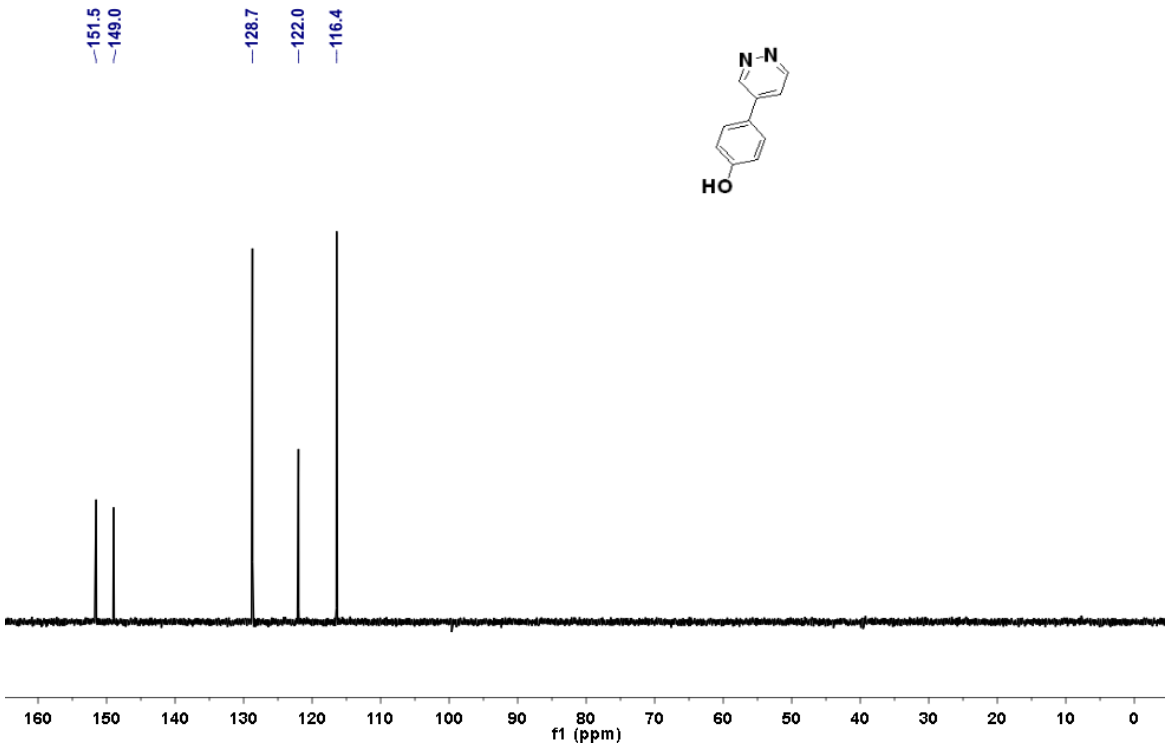
^{13}C DEPT 135-NMR of **4s** (15 mg) in 0.7 mL $CDCl_3$ at 297 K (δ in ppm).



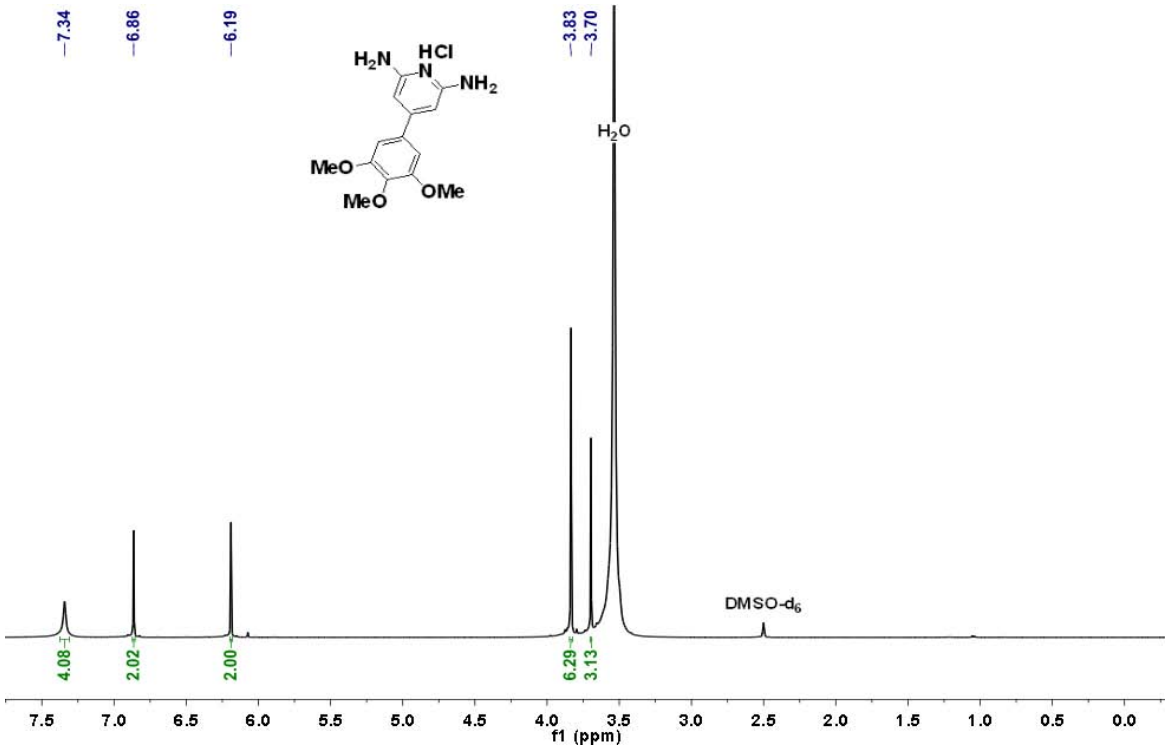
^{1}H NMR of **4t** (20 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm). *Impurities from residual solvents.



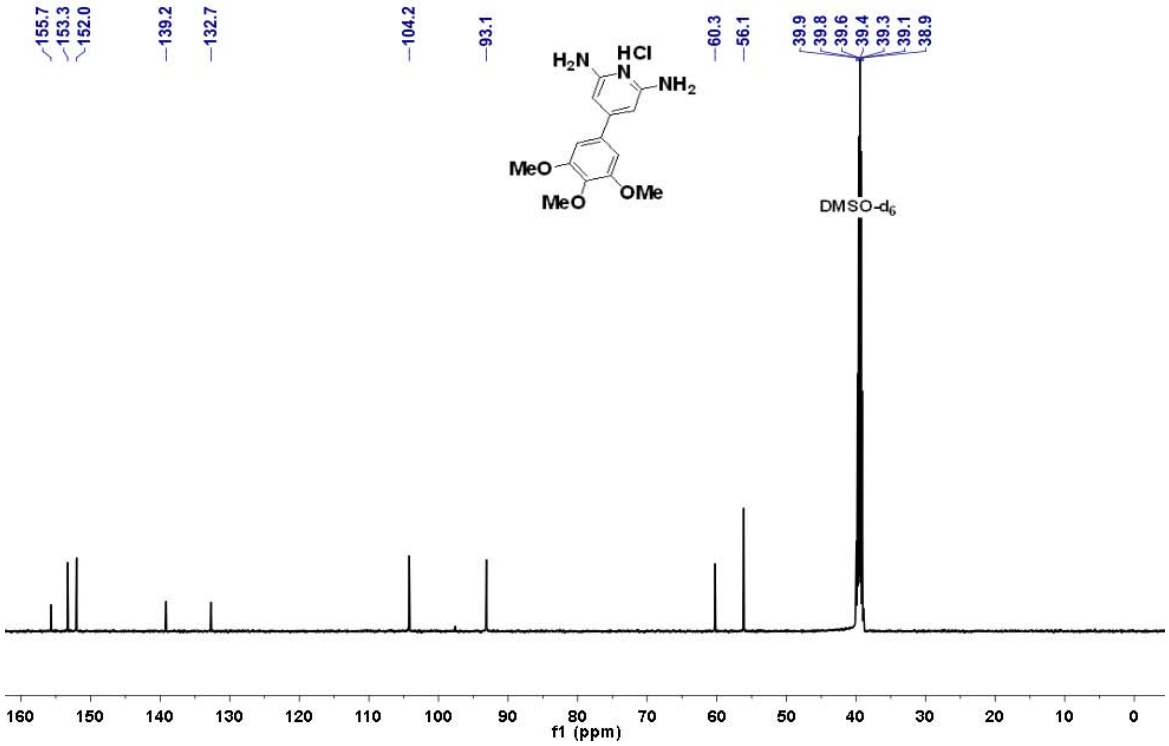
^{13}C NMR of **4t** (20 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



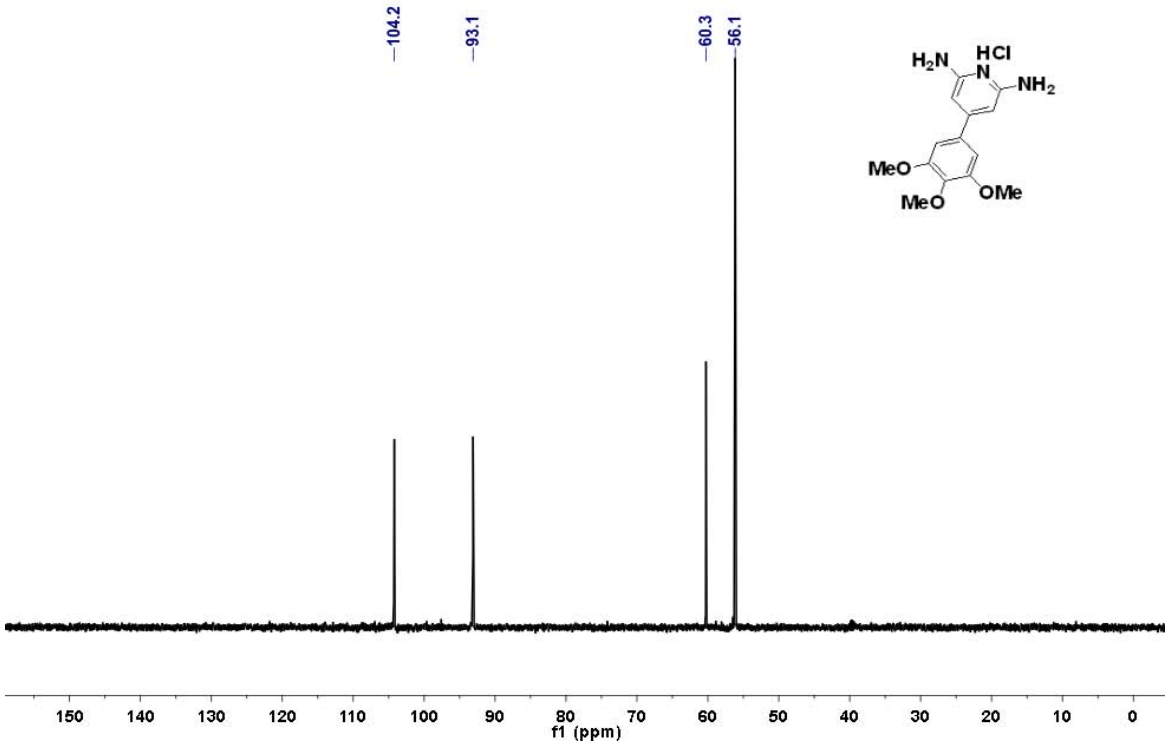
^{13}C DEPT 135-NMR of **4t** (20 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).



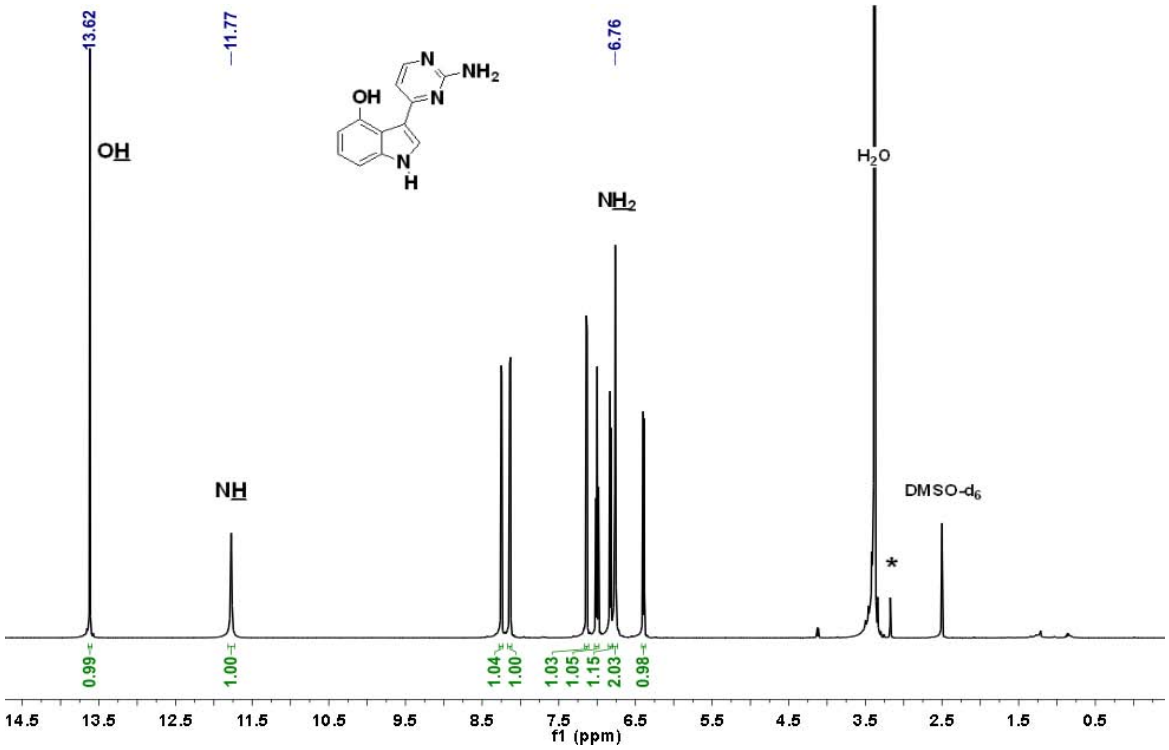
^{1}H NMR of **4u** (20 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



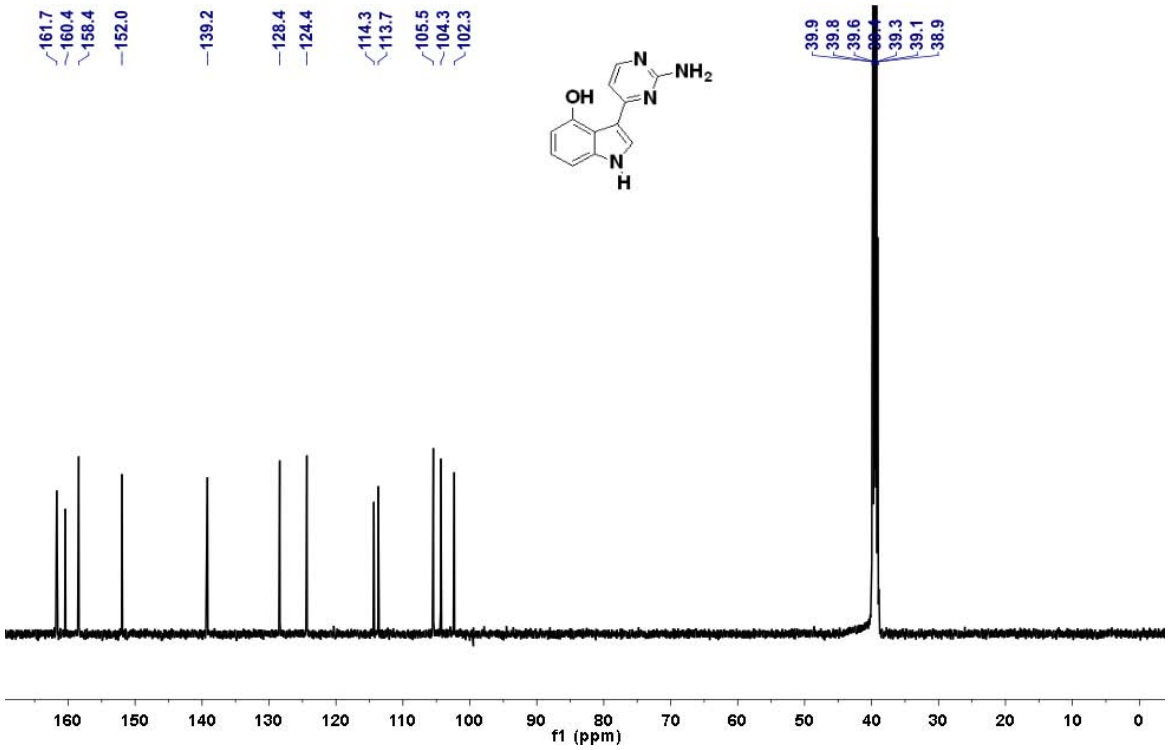
^{13}C NMR of **4u** (20 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



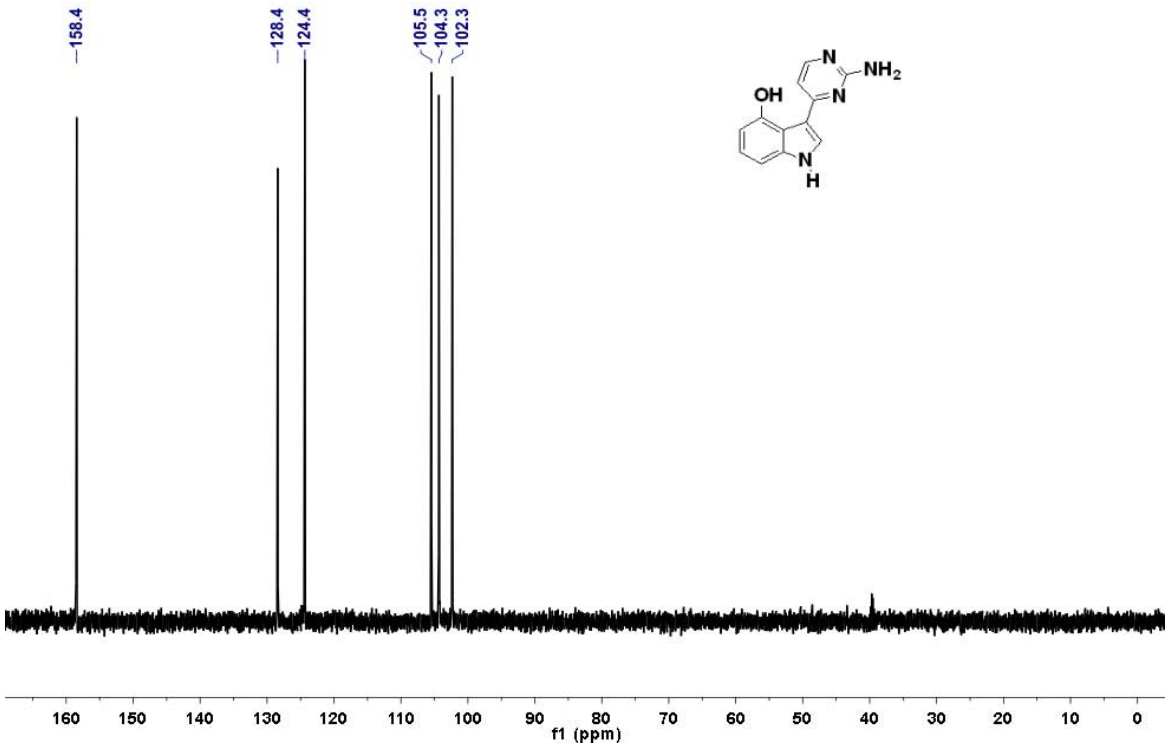
^{13}C DEPT 135-NMR of **4u** (20 mg) in 0.7 mL DMSO-d_6 at 296 K (δ in ppm).



^{1}H NMR of **5** (30 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm). *Impurities from residual solvents.



^{13}C NMR of **5** (30 mg) in 0.7 mL DMSO-d_6 at 298 K (δ in ppm).

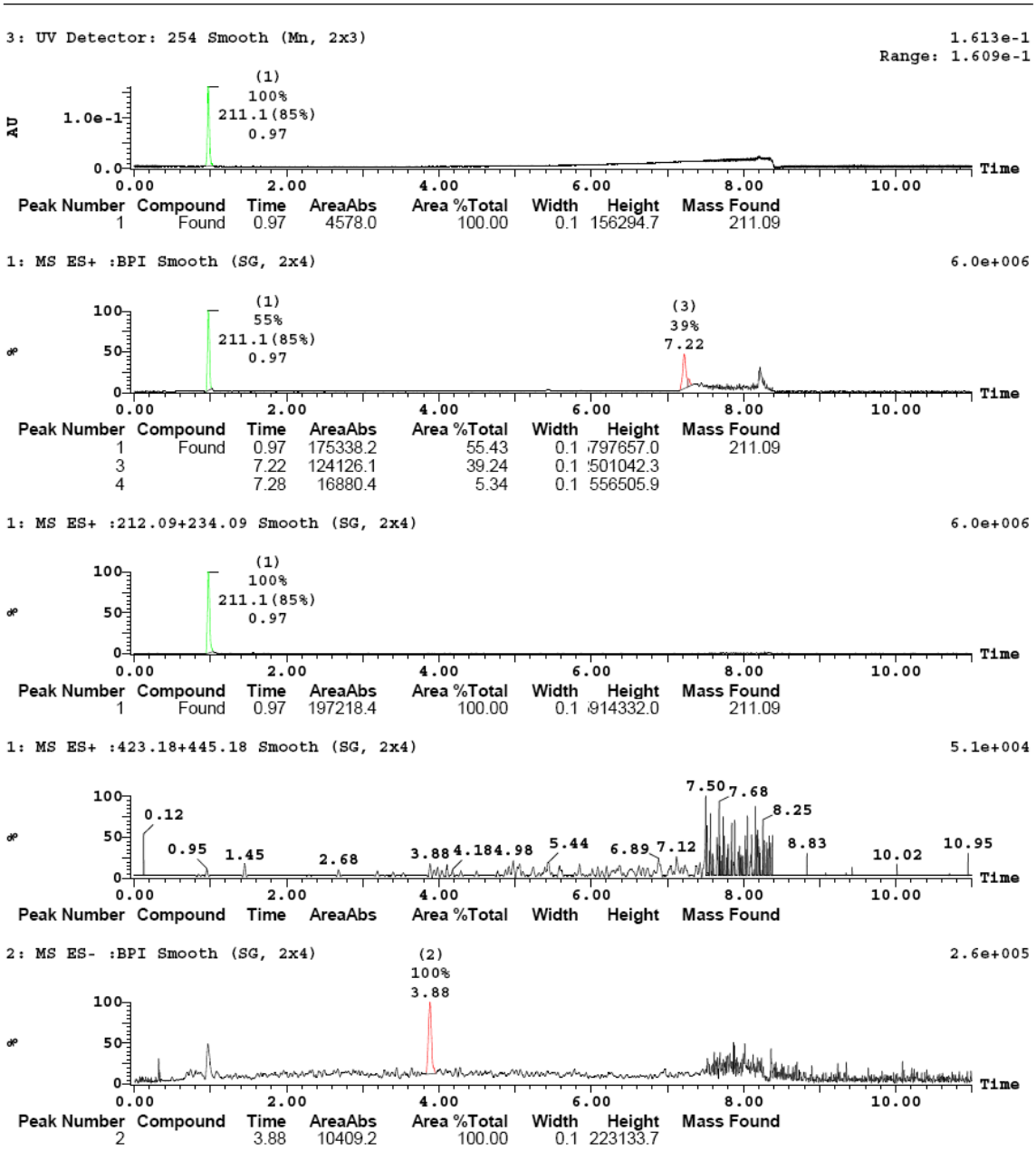


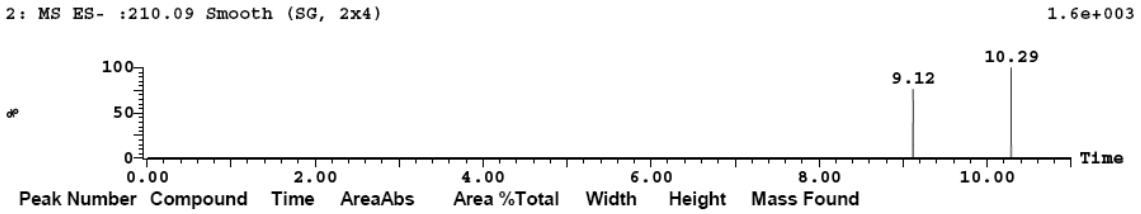
^{13}C DEPT 135-NMR of **5** (30 mg) in 0.7 mL DMSO-d_6 at 297 K (δ in ppm).

6. Appendix

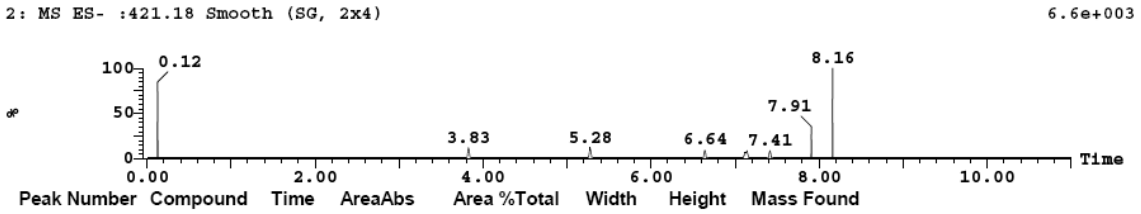
6.1. UV Purity of Compounds 4a-u and 5

HT-LC-MS Spectrum (SOP 2200) of **4a**. UV purity: 100 %





Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found



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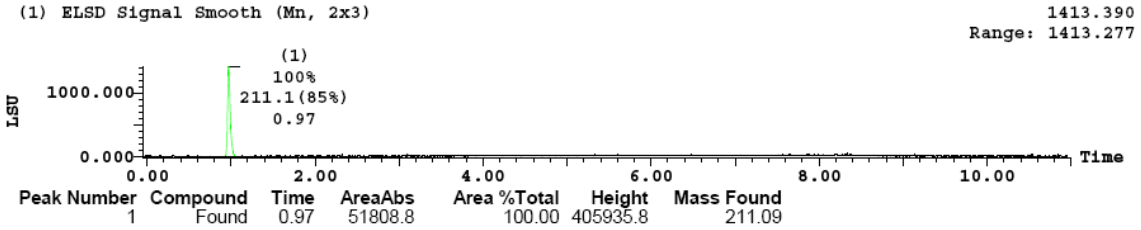

Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
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Peak ID	Compound	Time	Mass Found
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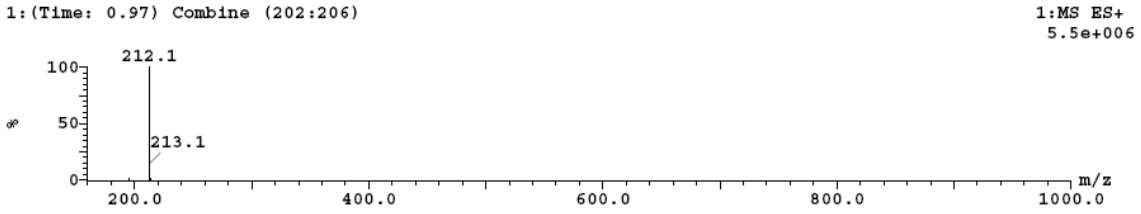
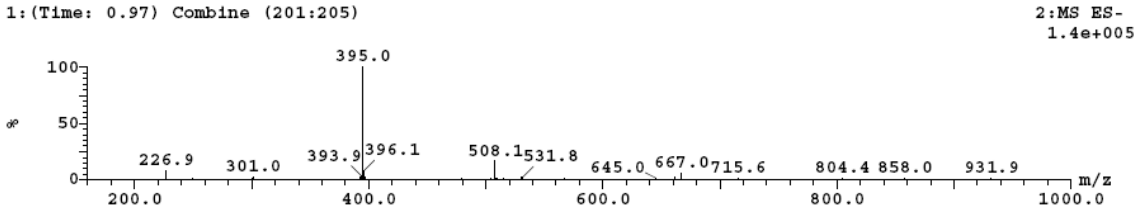


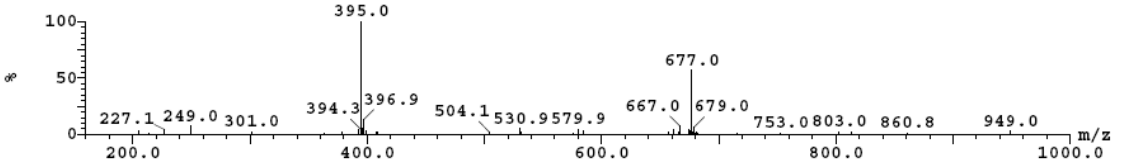
Peak ID	Compound	Time	Mass Found
1		0.97	



Peak ID	Compound	Time	Mass Found
2		3.88	

2:(Time: 3.88) Combine (810:814)

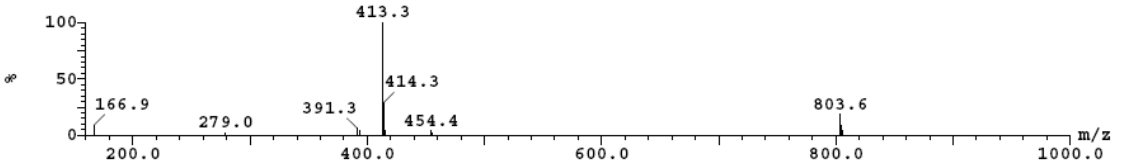
2:MS ES-
3.0e+005



Peak ID	Compound	Time	Mass Found
3		7.22	

3:(Time: 7.22) Combine (1508:1512)

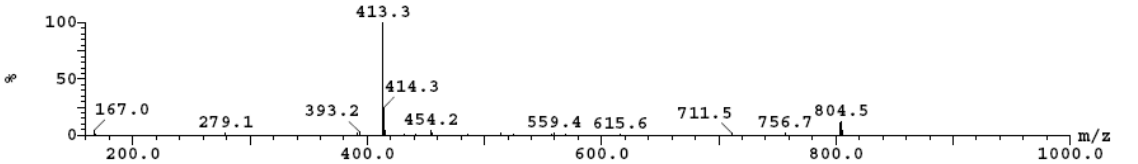
1:MS ES+
3.0e+006



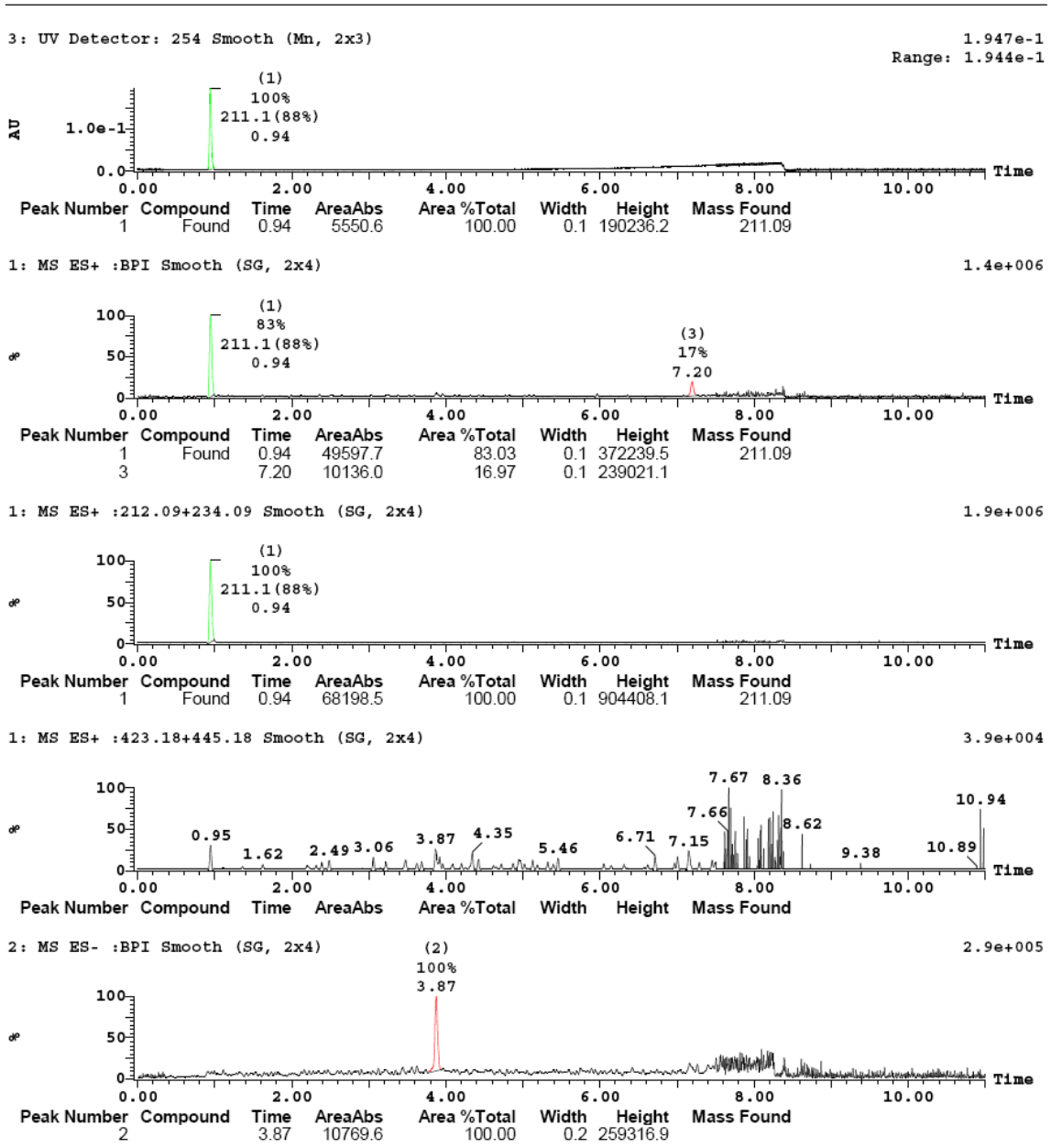
Peak ID	Compound	Time	Mass Found
4		7.28	

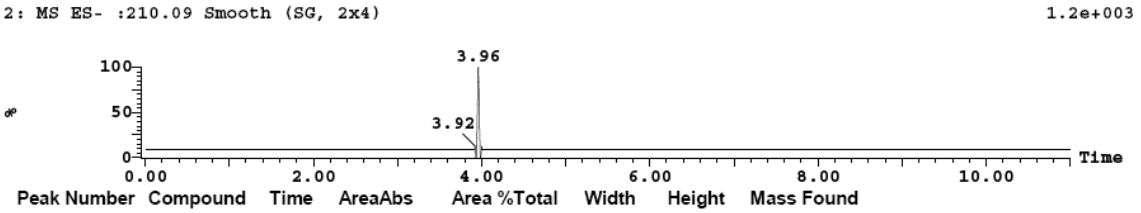
4:(Time: 7.28) Combine (1520:1524)

1:MS ES+
1.3e+006

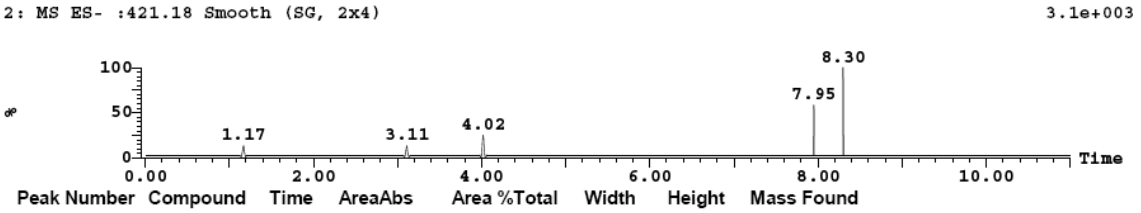


HT-LC-MS Spectrum (SOP 2200) of **4b**. UV purity: 100%

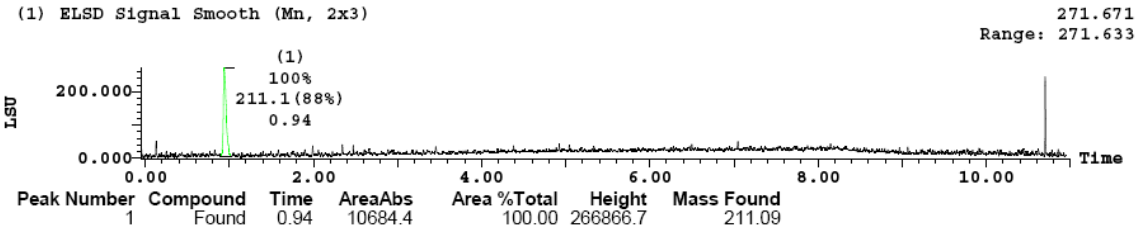




Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found

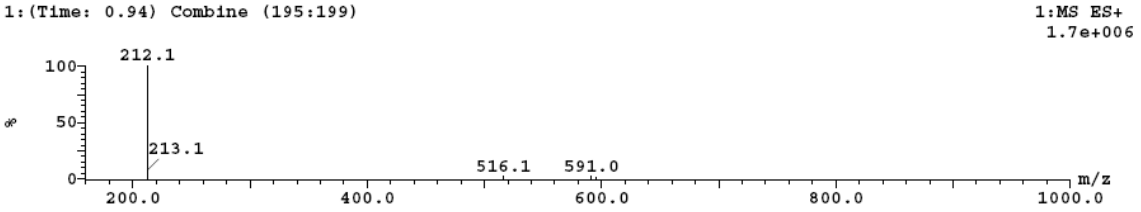


Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found

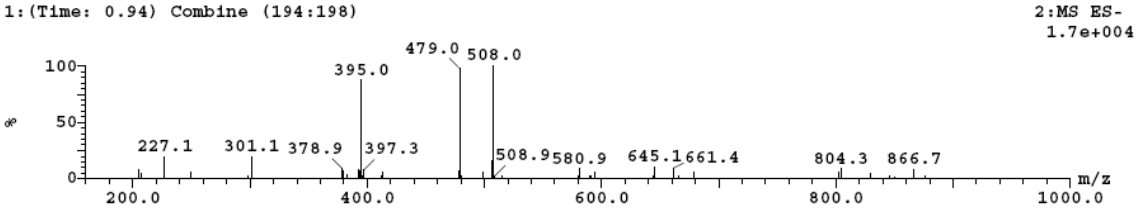


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	0.94	10684.4	100.00	266866.7	211.09

Peak ID	Compound	Time	Mass Found
1	Found	0.94	211.09

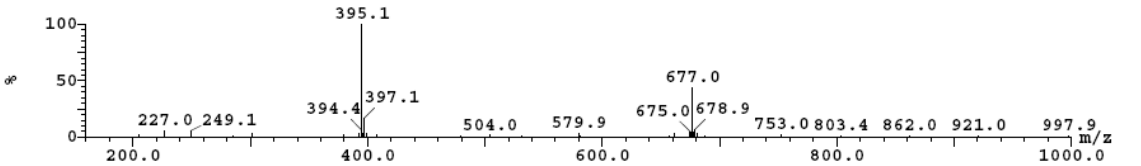


Peak ID	Compound	Time	Mass Found
1		0.94	



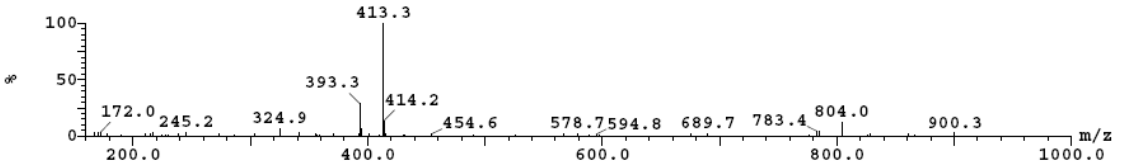
Peak ID	Compound	Time	Mass Found
2		3.87	

2:(Time: 3.87) Combine (808:812)

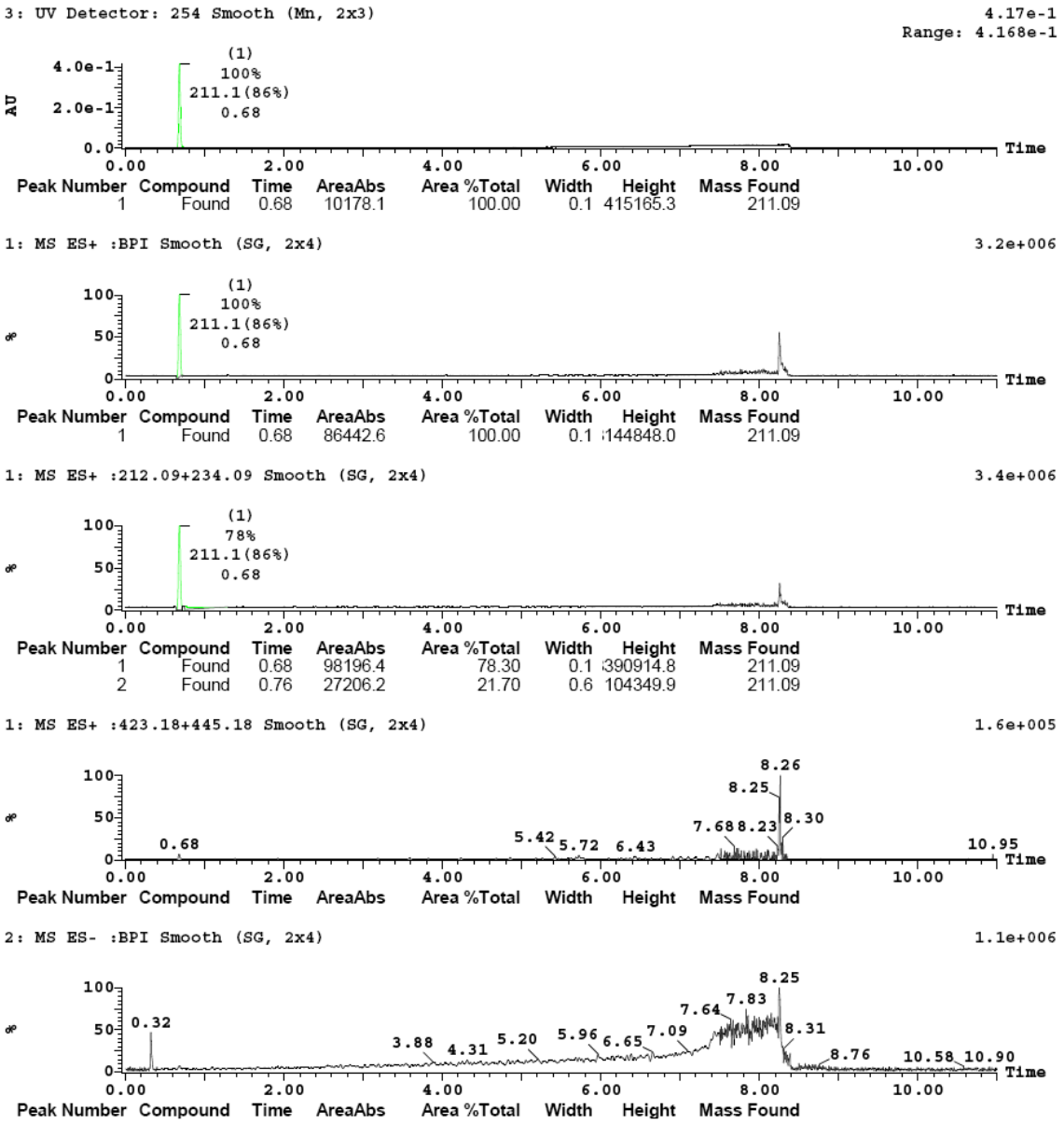


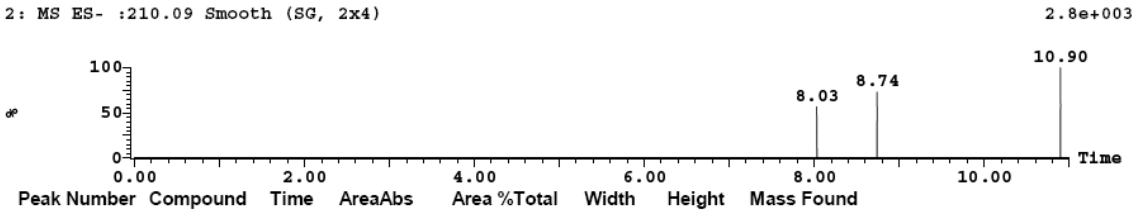
Peak ID	Compound	Time	Mass Found
3		7.20	

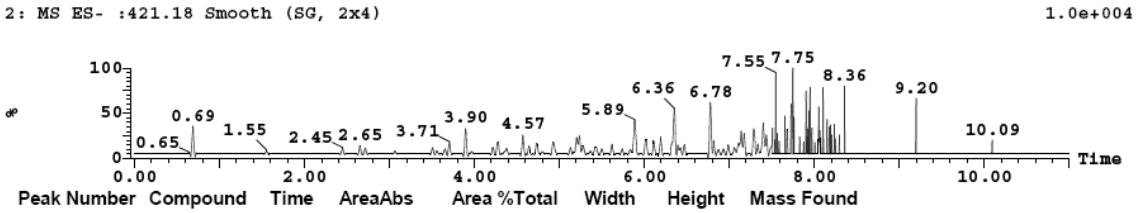
3:(Time: 7.20) Combine (1503:1507)

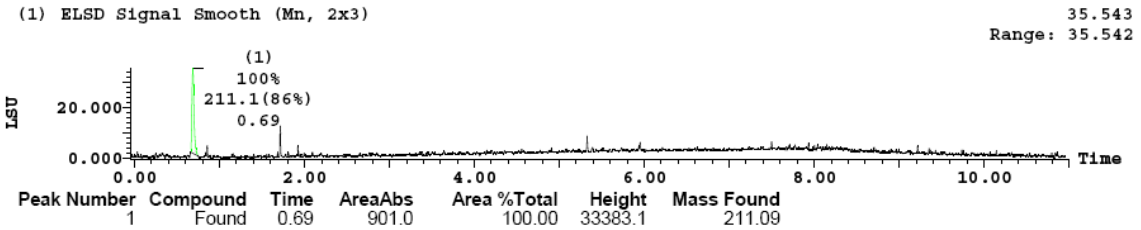


HT-LC-MS Spectrum (SOP 2200) of **4c**. UV purity: 100 %

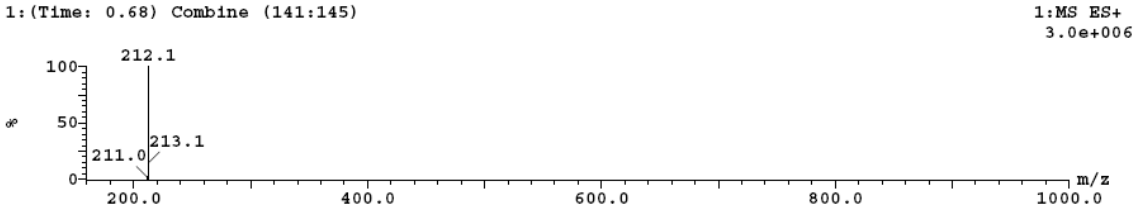




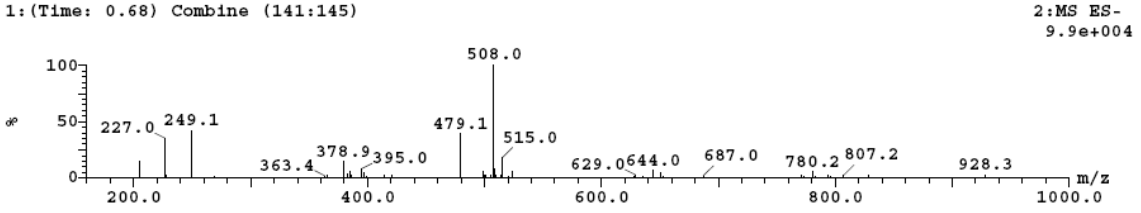




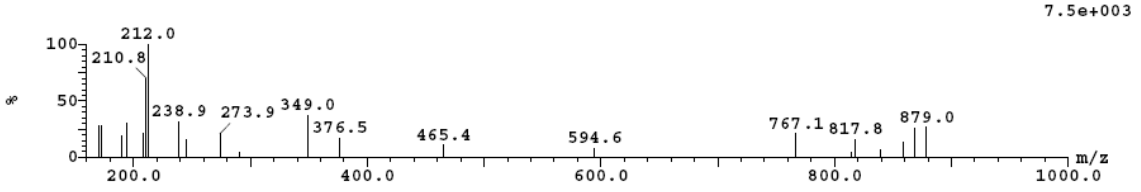
Peak ID Compound Time Mass Found
1 Found 0.68 211.09



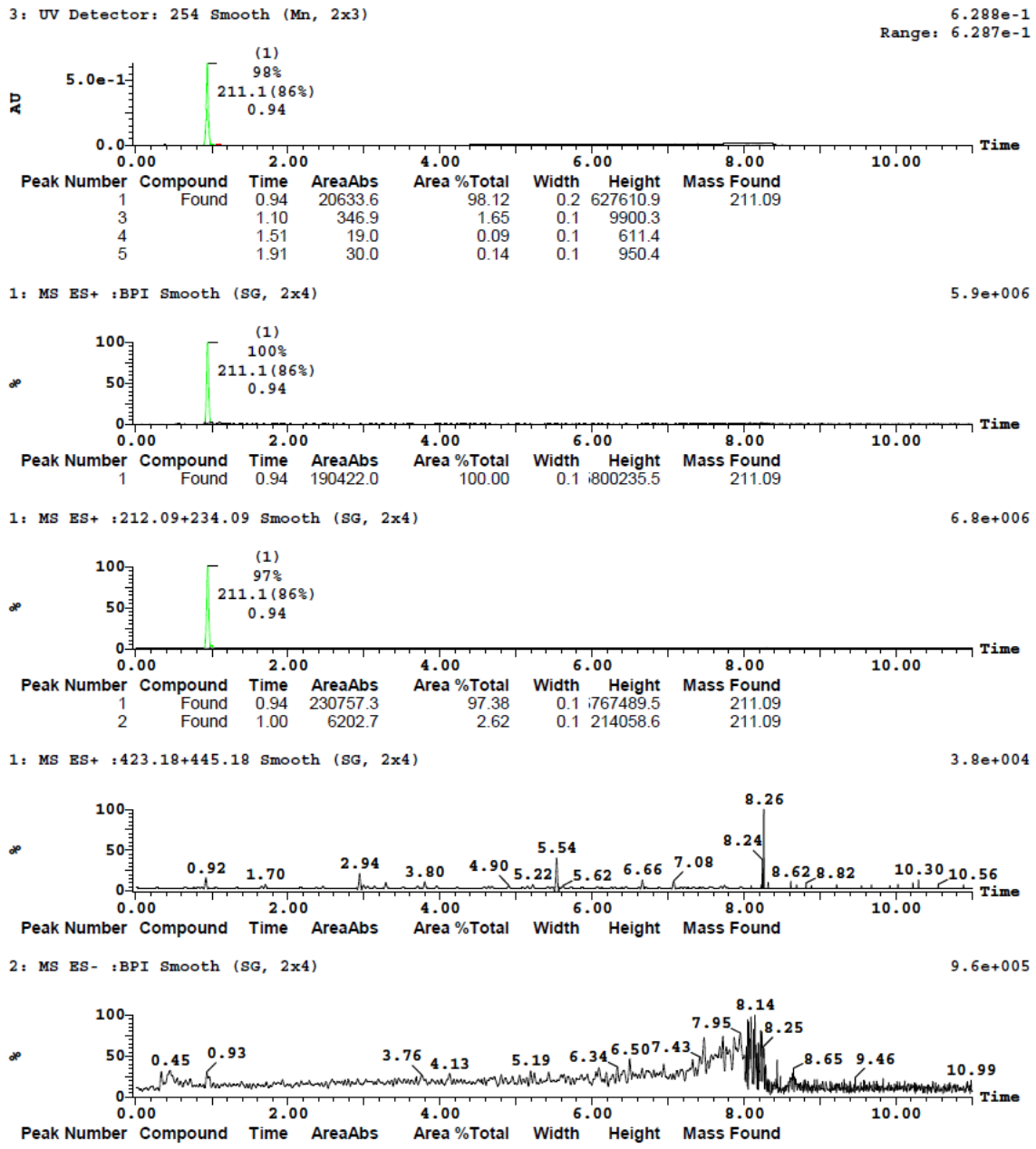
Peak ID Compound Time Mass Found
1 0.68

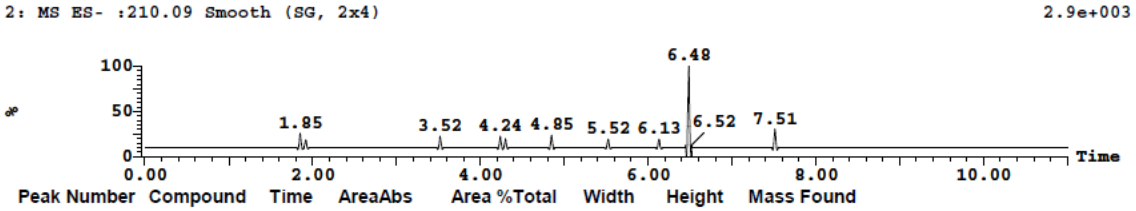


Peak ID Compound Time Mass Found
2 Found 0.76 211.09

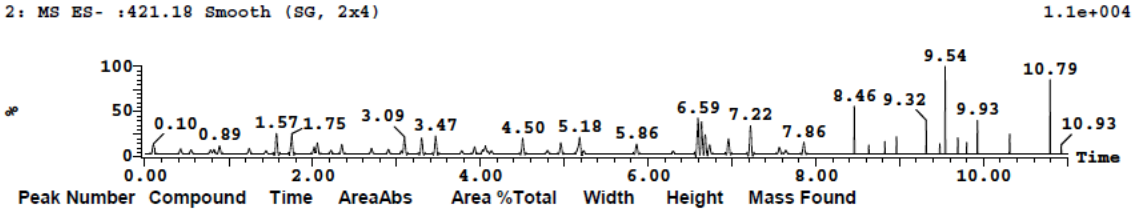


HT-LC-MS Spectrum (SOP 2200) of **4d**. UV purity: 98.1 %

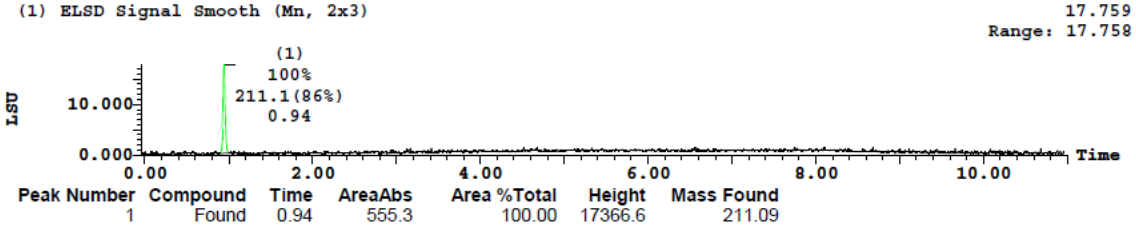




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found



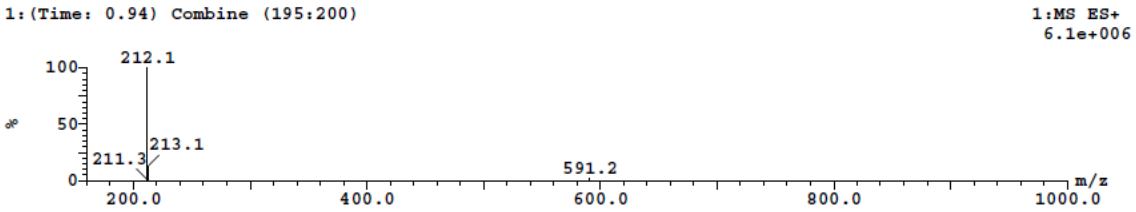
Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found



Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	0.94	555.3	100.00	17366.6	211.09

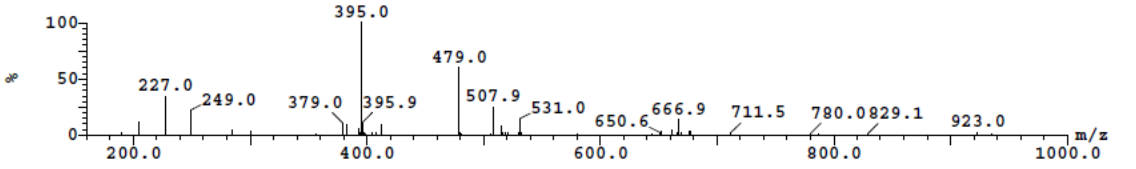
Peak ID	Compound	Time	Mass Found
1	Found	0.94	211.09

1:(Time: 0.94) Combine (195:200)



Peak ID	Compound	Time	Mass Found
1		0.94	

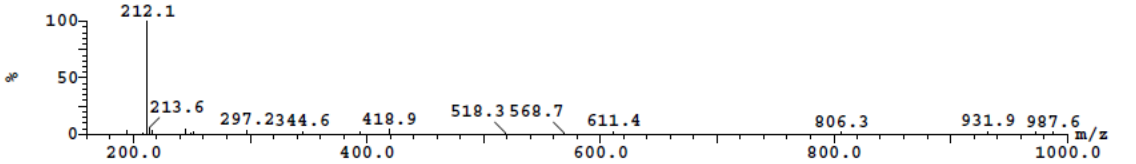
1:(Time: 0.94) Combine (195:199)



Peak ID	Compound	Time	Mass Found
2	Found	1.00	211.09

2:(Time: 1.00) Combine (207:211)

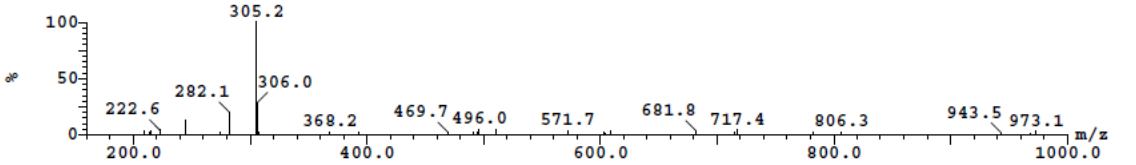
1:MS ES+
2.4e+005



Peak ID	Compound	Time	Mass Found
3		1.10	

3:(Time: 1.10) Combine (228:232)

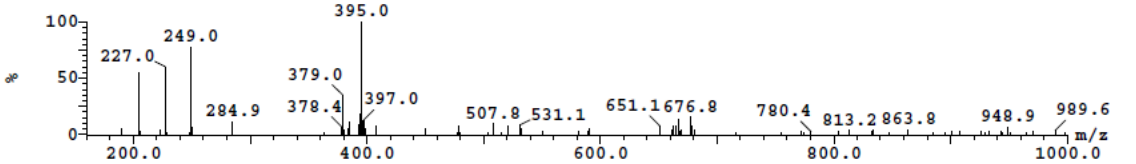
1:MS ES+
1.7e+005



Peak ID	Compound	Time	Mass Found
3		1.10	

3:(Time: 1.10) Combine (228:232)

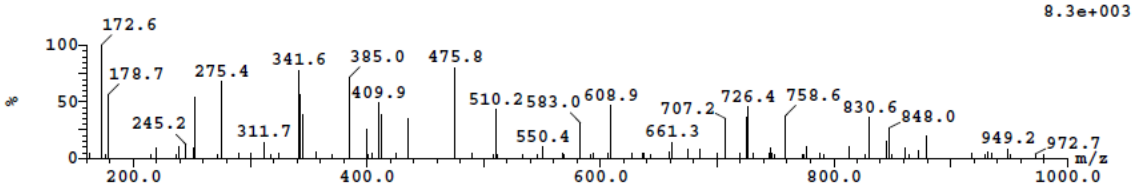
2:MS ES-
1.2e+005

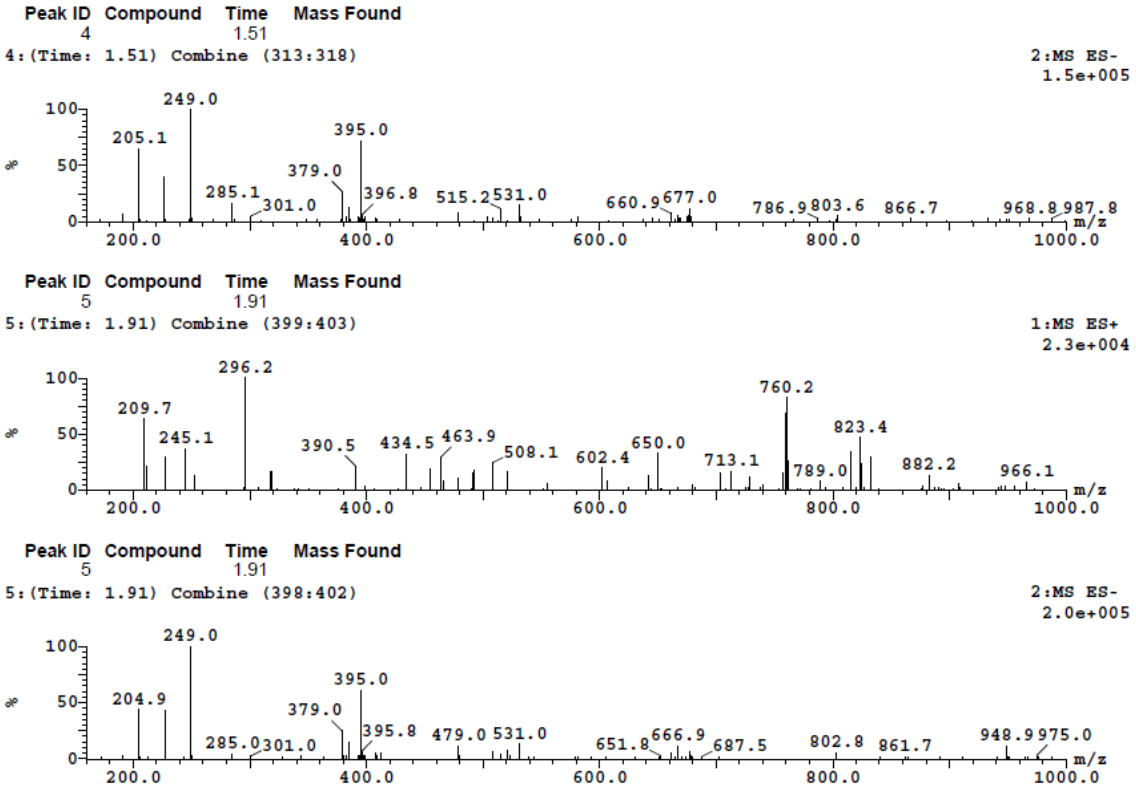


Peak ID	Compound	Time	Mass Found
4		1.51	

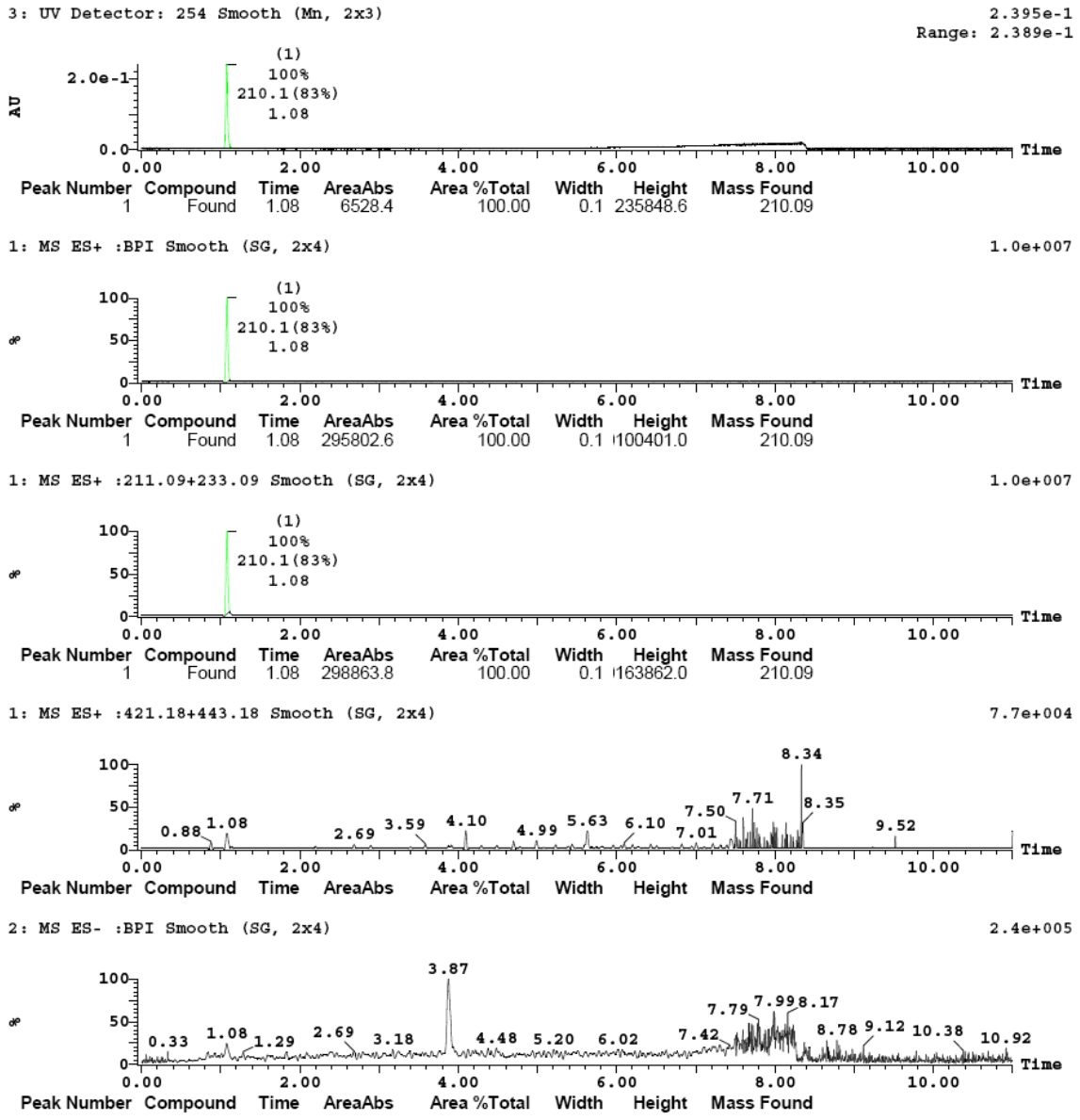
4:(Time: 1.51) Combine (314:318)

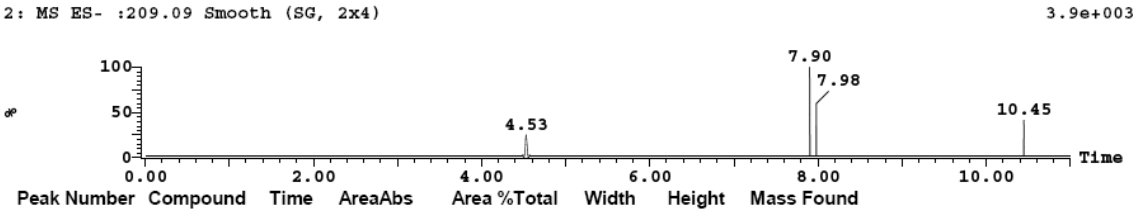
1:MS ES+
8.3e+003



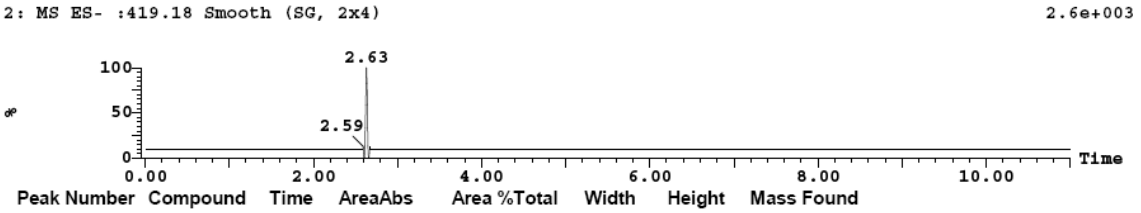

Peak ID Compound Time Mass Found
4 1.51
4:(Time: 1.51) Combine (313:318)
2:MS ES-
1.5e+005
249.0
205.1
395.0
379.0
285.1
301.0
396.8
515.2
531.0
660.9
677.0
786.9
803.6
866.7
968.8
987.8
m/z
Peak ID Compound Time Mass Found
5 1.91
5:(Time: 1.91) Combine (399:403)
1:MS ES+
2.3e+004
296.2
209.7
245.1
390.5
434.5
463.9
508.1
602.4
650.0
713.1
760.2
789.0
823.4
882.2
966.1
m/z
Peak ID Compound Time Mass Found
5 1.91
5:(Time: 1.91) Combine (398:402)
2:MS ES-
2.0e+005
249.0
204.9
395.0
379.0
285.0
301.0
395.8
479.0
531.0
651.8
666.9
687.5
802.8
861.7
948.9
975.0
m/z

HT-LC-MS Spectrum (SOP 2200) of **4e**. UV purity: 100 %

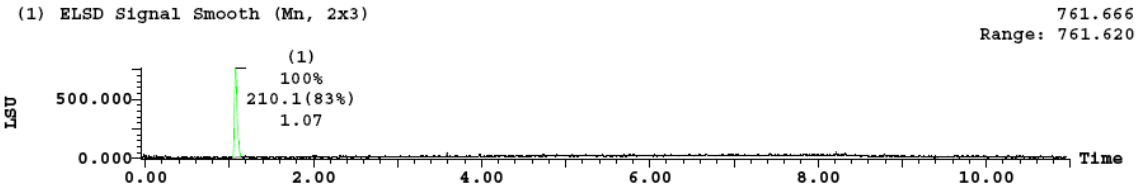




Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

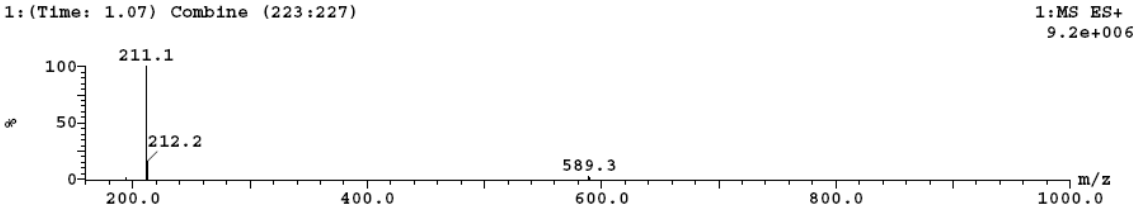


Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

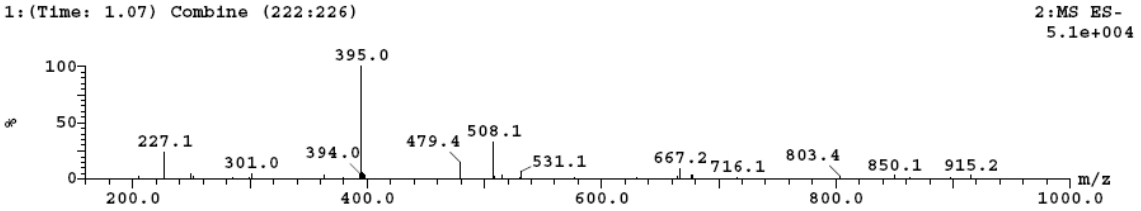


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	1.07	27974.8	100.00	752338.2	210.09

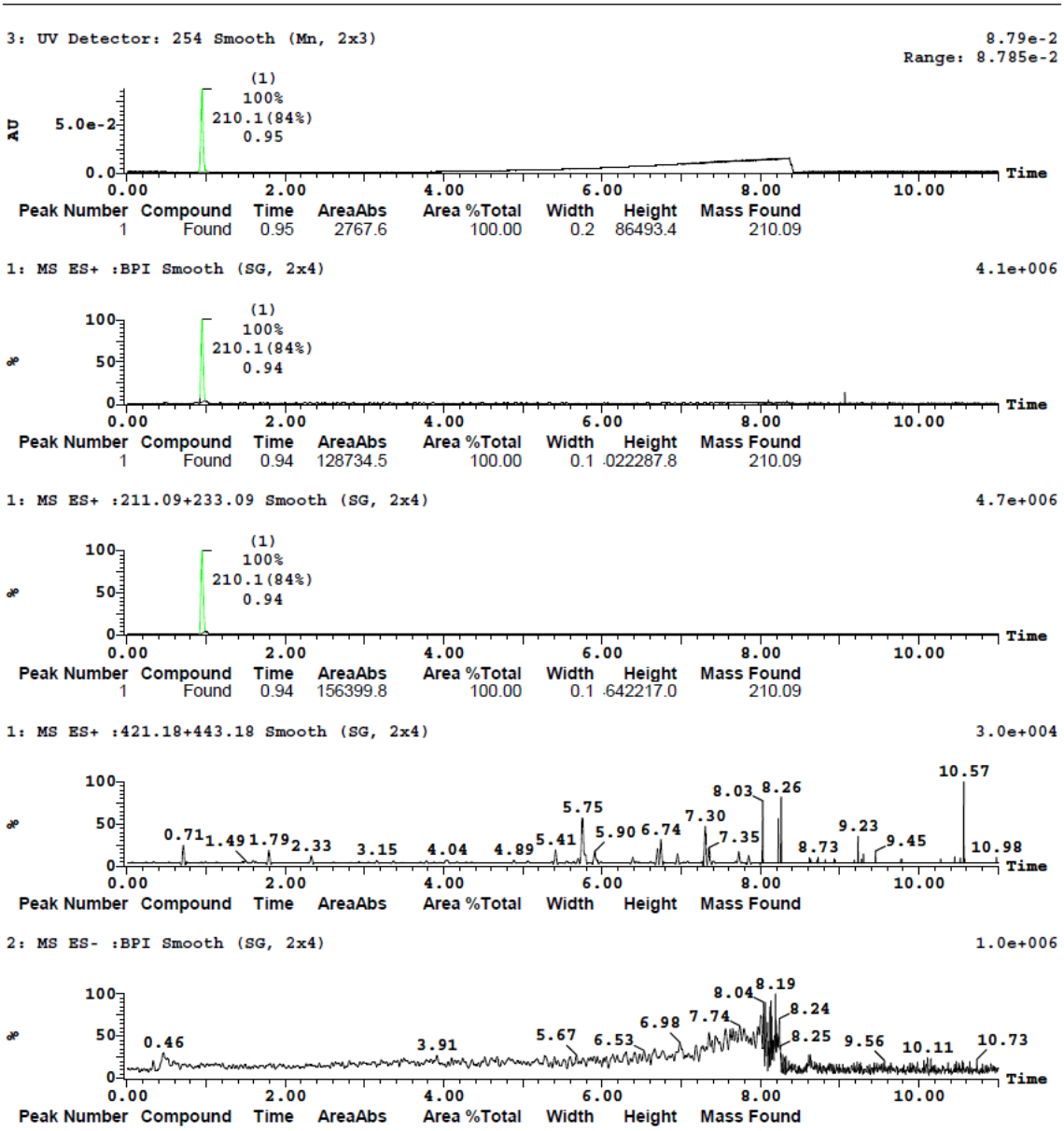
Peak ID	Compound	Time	Mass Found
1	Found	1.08	210.09

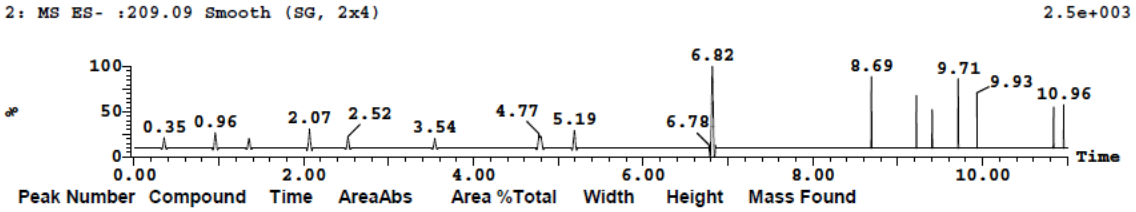


Peak ID	Compound	Time	Mass Found
1		1.08	

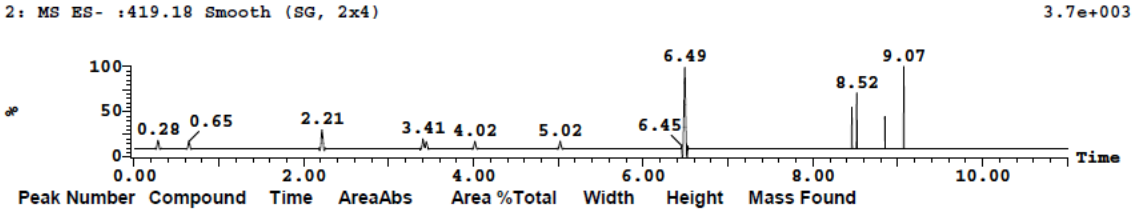


HT-LC-MS Spectrum (SOP 2200) of **4f**. UV purity: 100 %

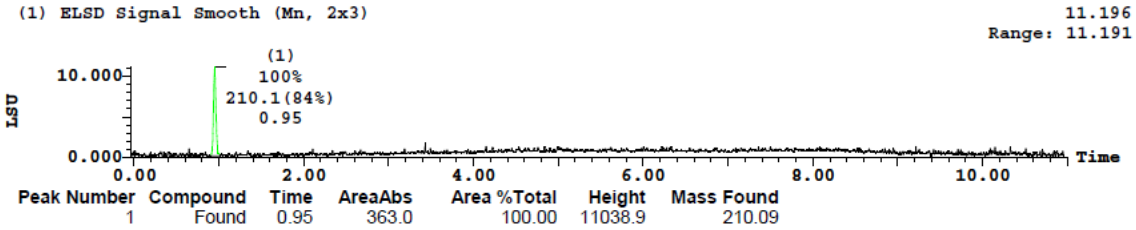




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

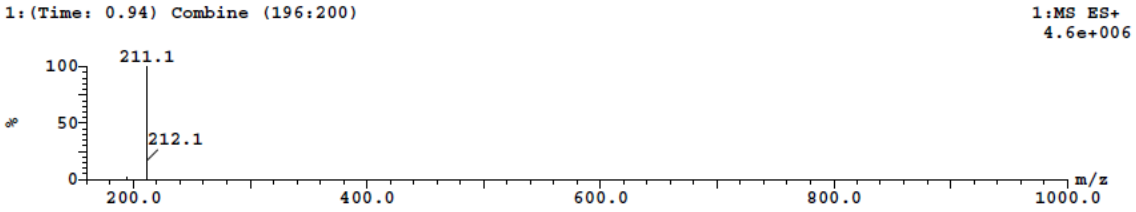


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

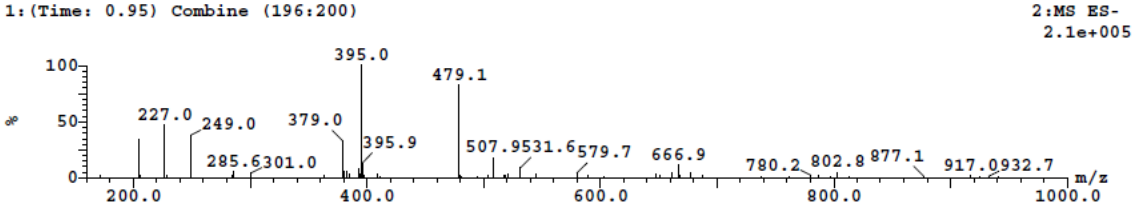


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	0.95	363.0	100.00	11038.9	210.09

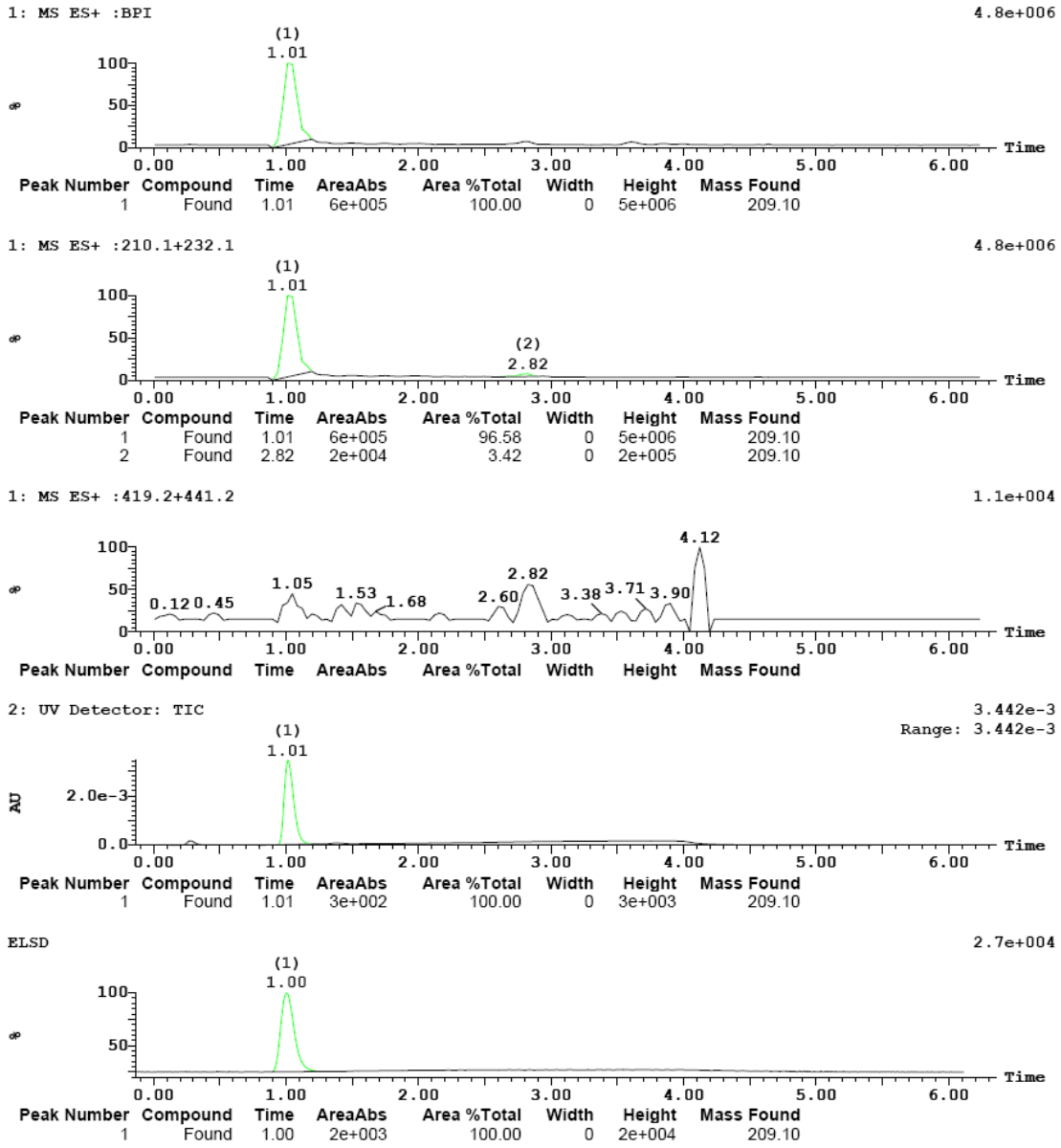
Peak ID	Compound	Time	Mass Found
1	Found	0.94	210.09



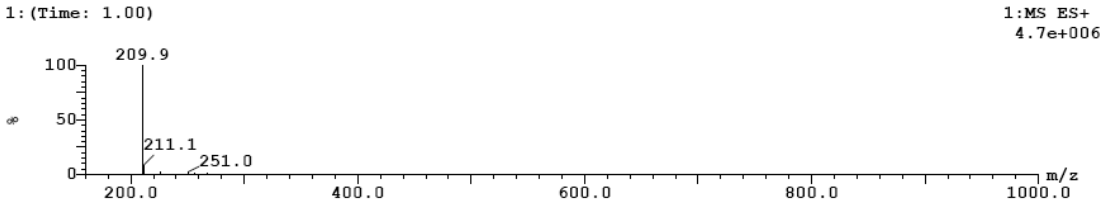
Peak ID	Compound	Time	Mass Found
1		0.94	



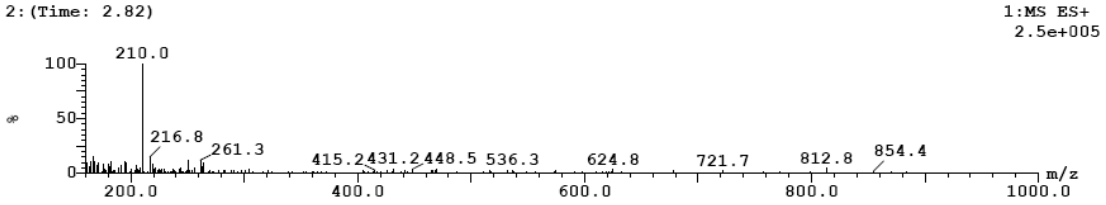
HT-LC-MS Spectrum (SOP 2222) of **4g**. UV purity: 100 %



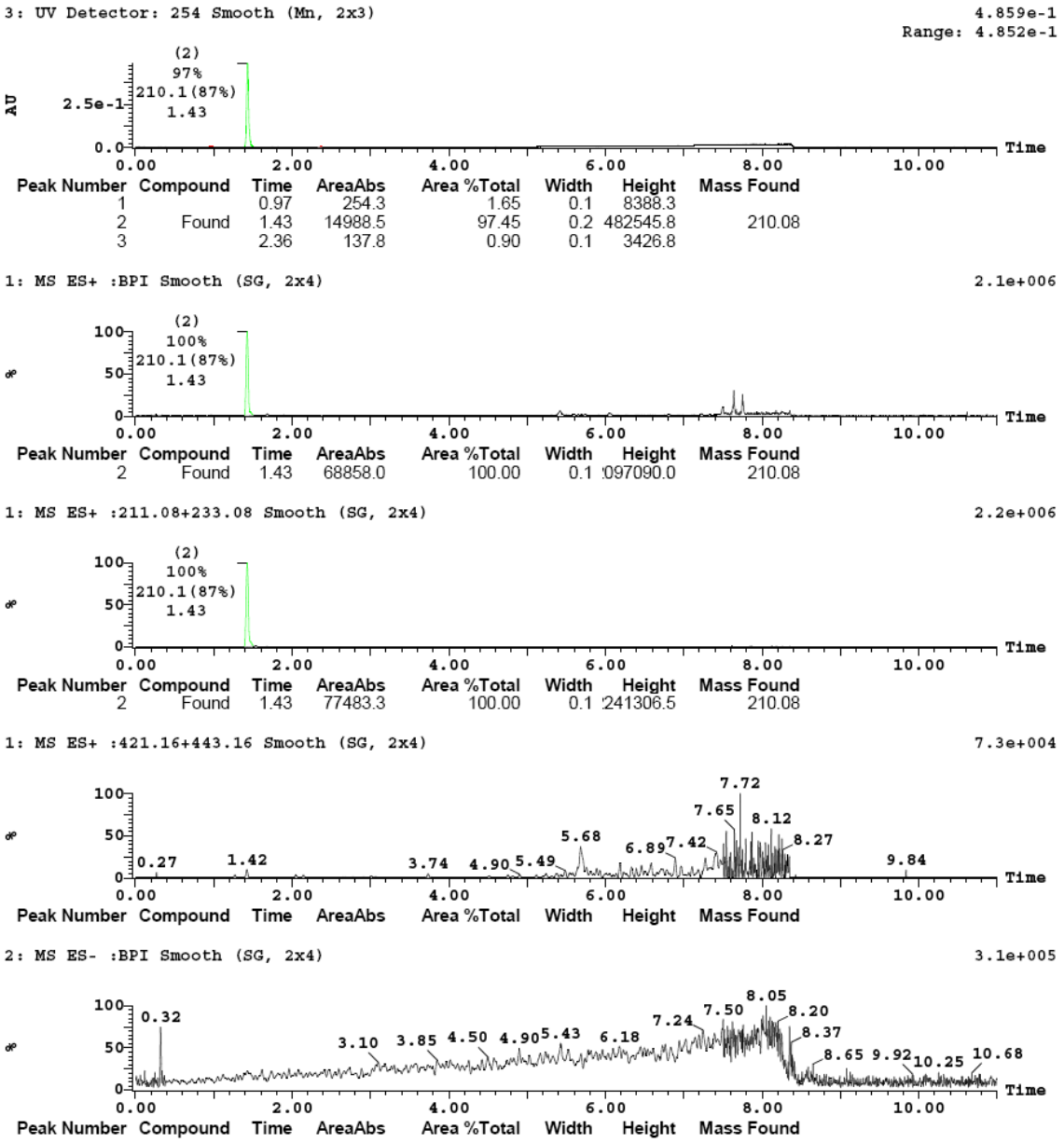
Peak ID	Compound	Time	Mass Found
1	Found	1.01	209.10

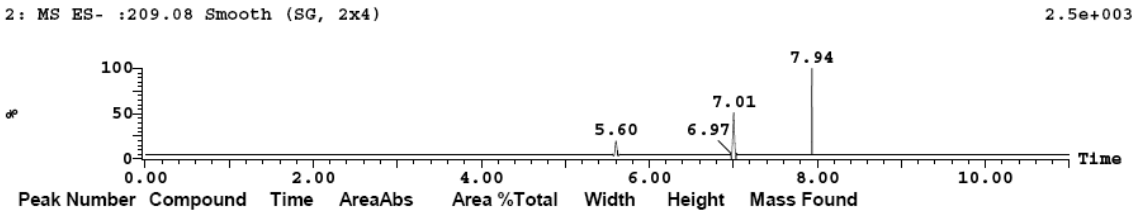


Peak ID	Compound	Time	Mass Found
2	Found	2.82	209.10

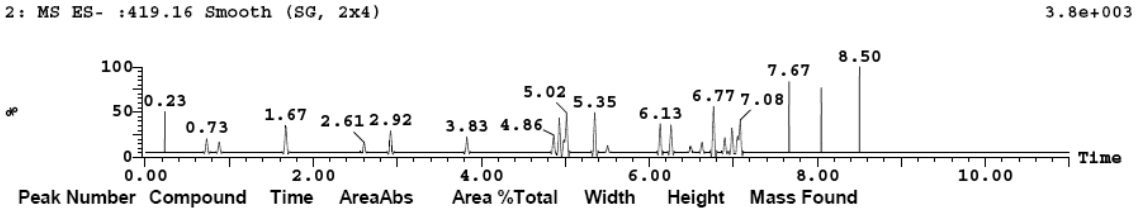


HT-LC-MS Spectrum (SOP 2200) of **4h**. UV purity: 97.5 %

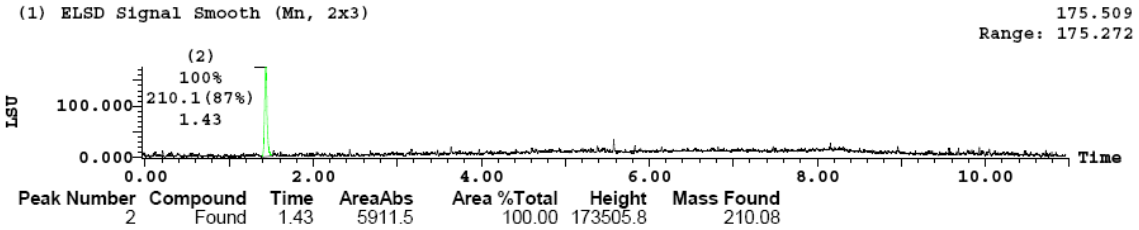




Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

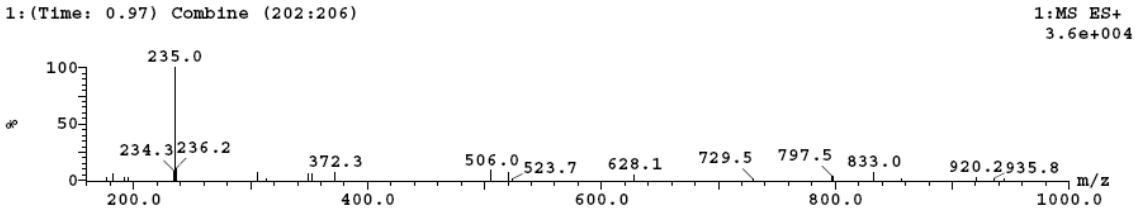


Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

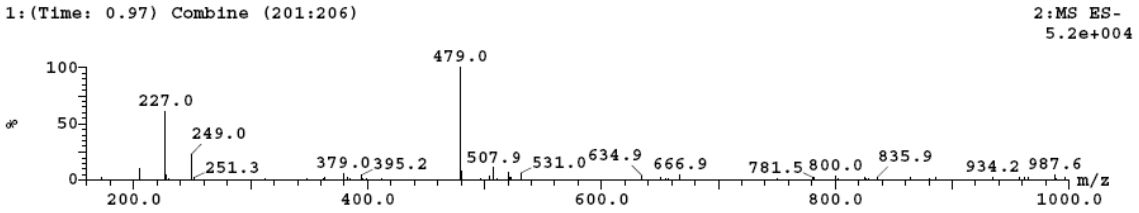


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
2	Found	1.43	5911.5	100.00	173505.8	210.08

Peak ID	Compound	Time	Mass Found
1		0.97	



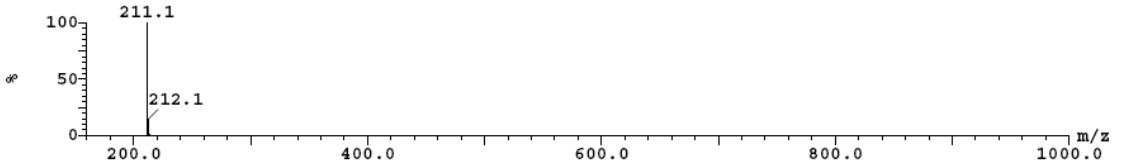
Peak ID	Compound	Time	Mass Found
1		0.97	



Peak ID	Compound	Time	Mass Found
2	Found	1.43	210.08

2:(Time: 1.43) Combine (297:301)

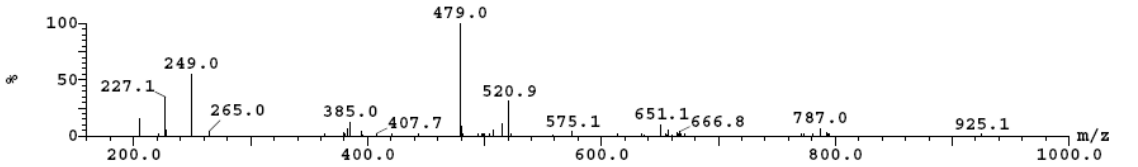
1:MS ES+
2.1e+006



Peak ID	Compound	Time	Mass Found
2		1.43	

2:(Time: 1.43) Combine (298:302)

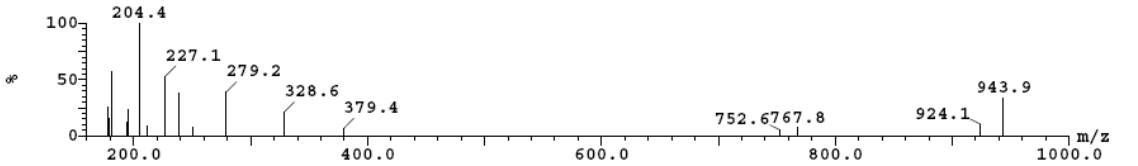
2:MS ES-
8.7e+004



Peak ID	Compound	Time	Mass Found
3		2.36	

3:(Time: 2.36) Combine (493:497)

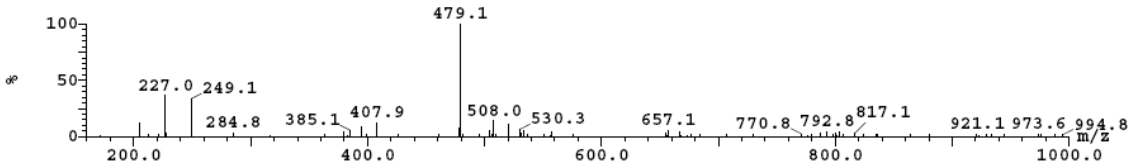
1:MS ES+
4.1e+003



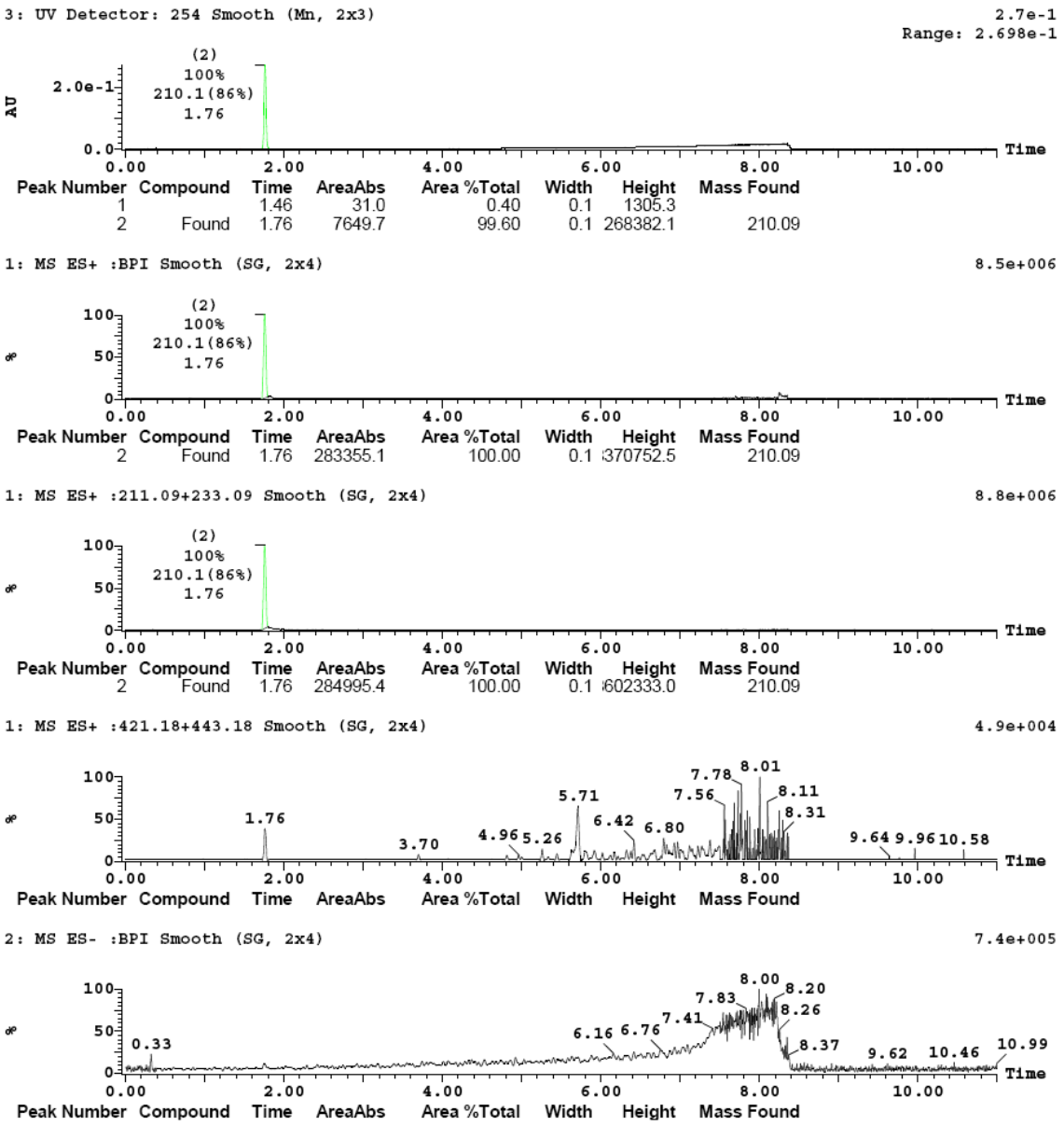
Peak ID	Compound	Time	Mass Found
3		2.36	

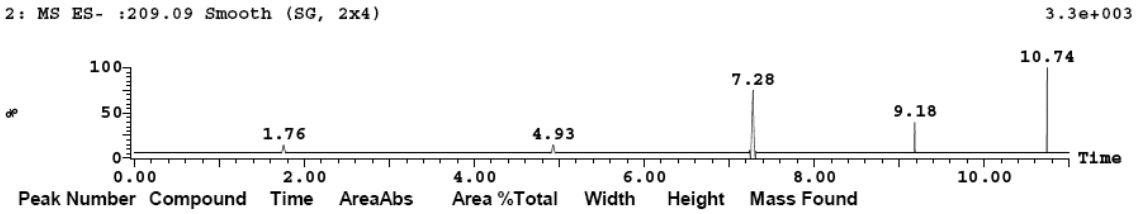
3:(Time: 2.36) Combine (492:497)

2:MS ES-
6.8e+004

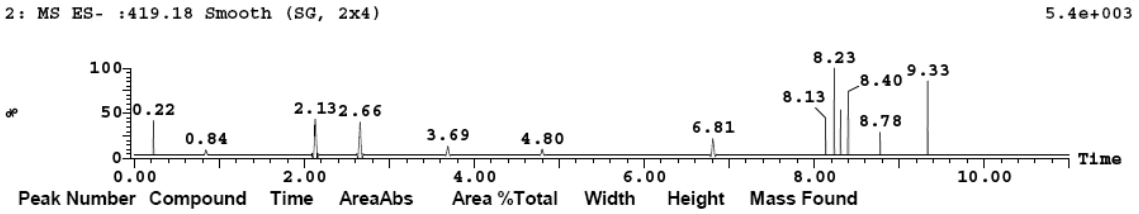


HT-LC-MS Spectrum (SOP 2200) of **4i**. UV purity: 99.6 %

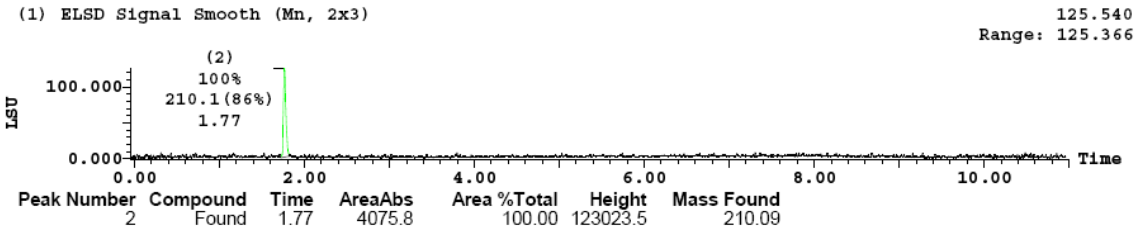




Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

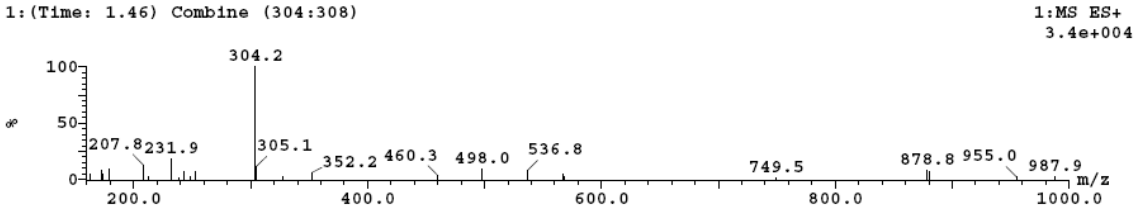


Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

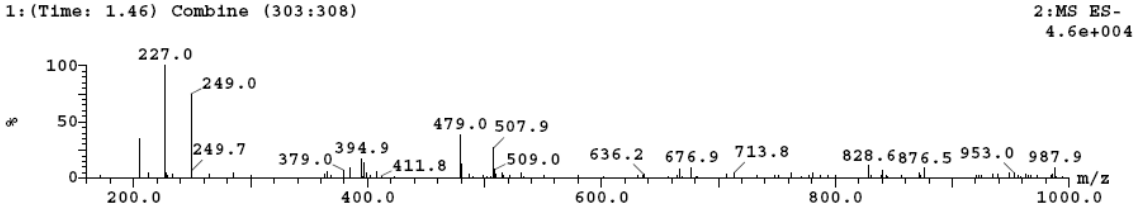


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
2	Found	1.77	4075.8	100.00	123023.5	210.09

Peak ID	Compound	Time	Mass Found
1		1.46	



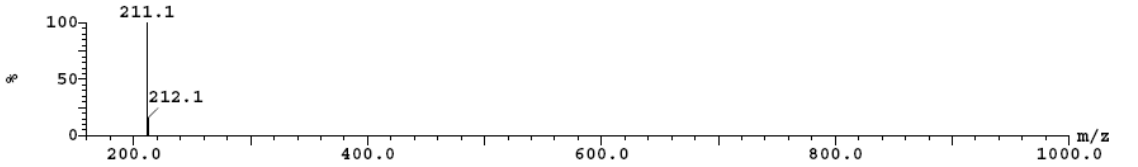
Peak ID	Compound	Time	Mass Found
1		1.46	



Peak ID	Compound	Time	Mass Found
2	Found	1.76	210.09

2:(Time: 1.76) Combine (366:370)

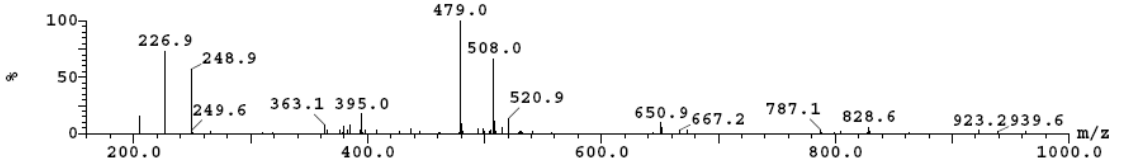
1:MS ES+
8.3e+006



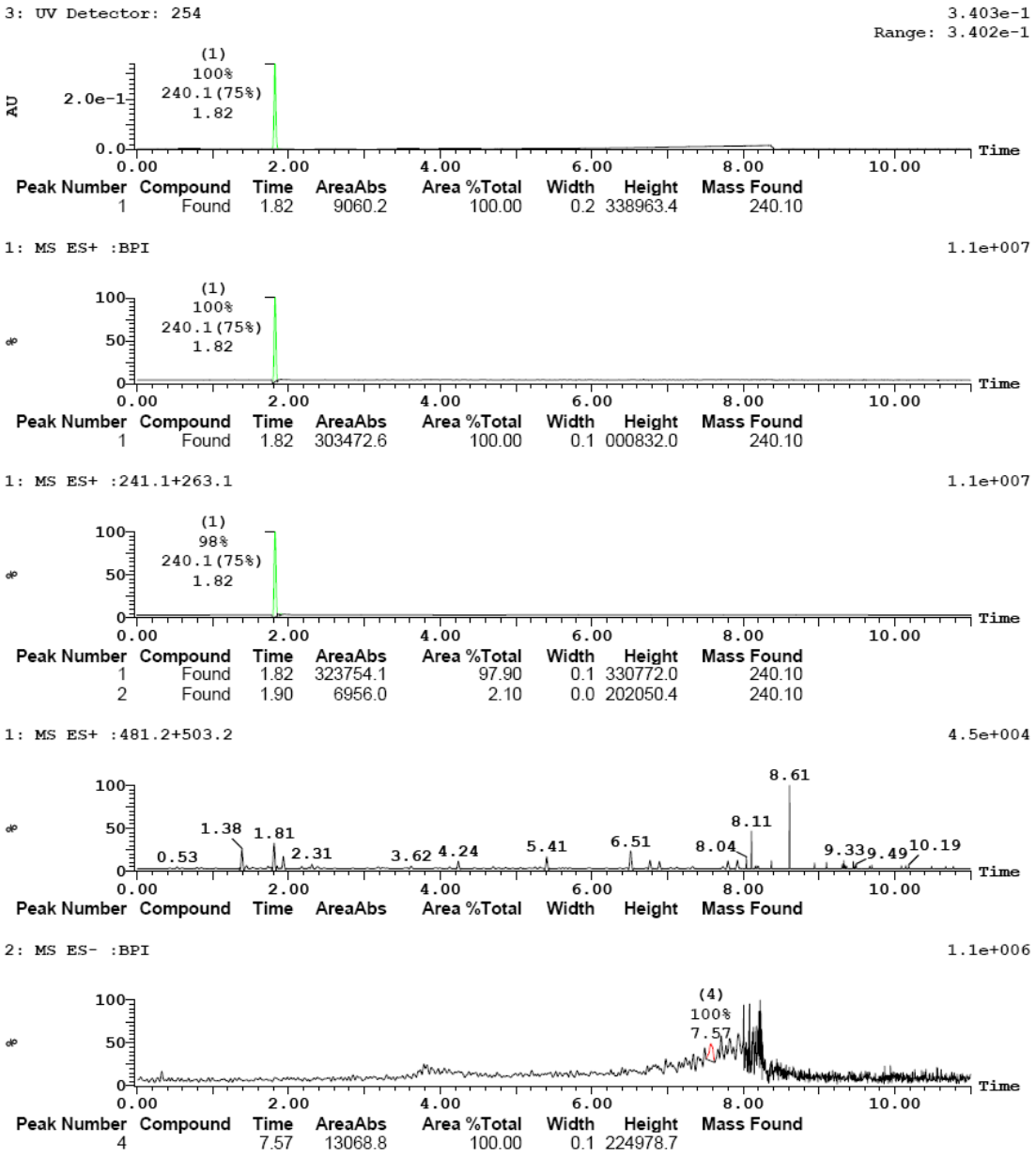
Peak ID	Compound	Time	Mass Found
2		1.76	

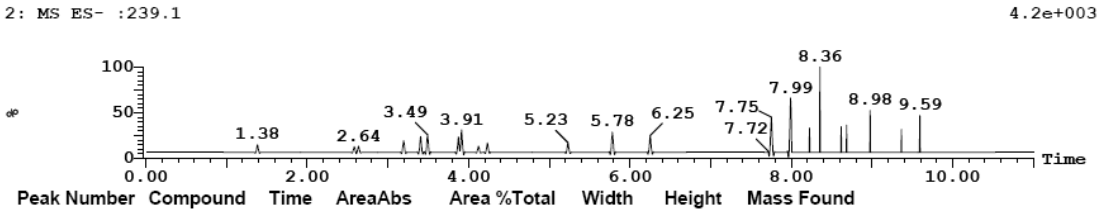
2:(Time: 1.77) Combine (367:371)

2:MS ES-
1.0e+005

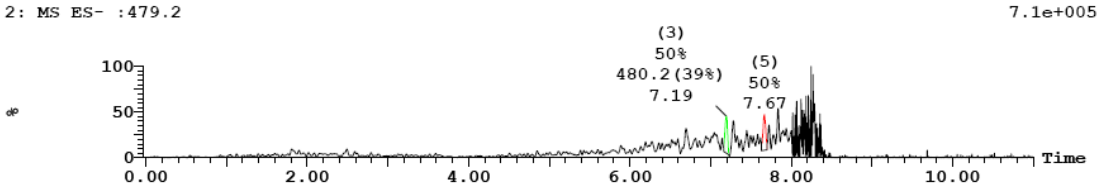


HT-LC-MS Spectrum (SOP 2200) of **4j**. UV purity: 100 %

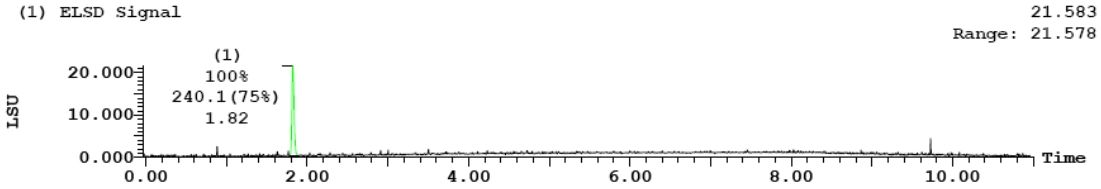




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

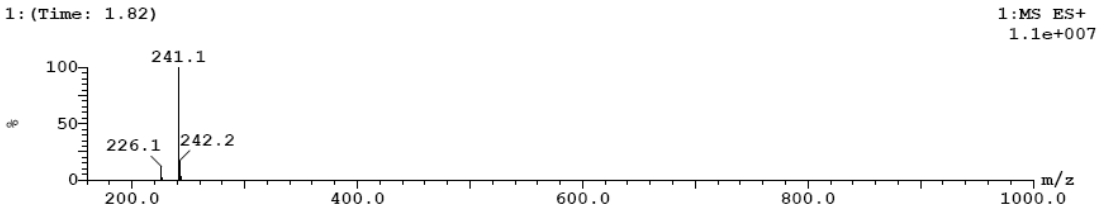


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
3	Found	7.19	10652.8	49.77	0.1	287871.5	480.20
5		7.67	10751.6	50.23	0.1	280238.9	

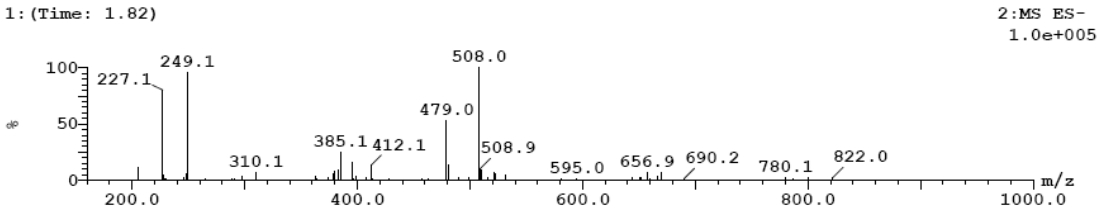


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	1.82	671.5	100.00	21220.9	240.10

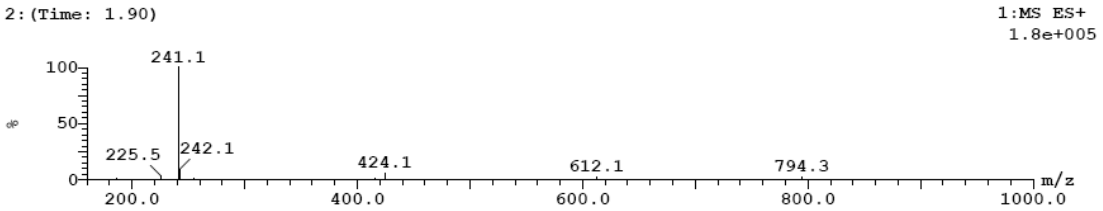
Peak ID	Compound	Time	Mass Found
1	Found	1.82	240.10



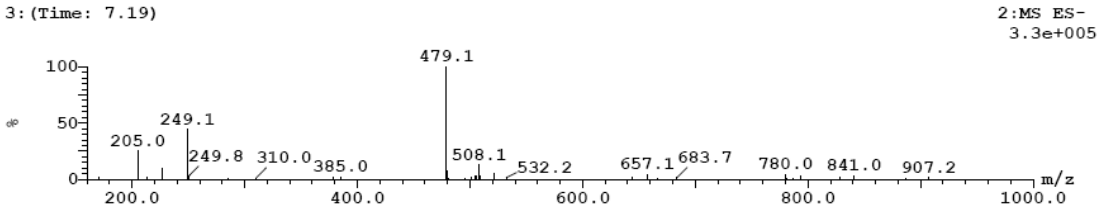
Peak ID	Compound	Time	Mass Found
1		1.82	



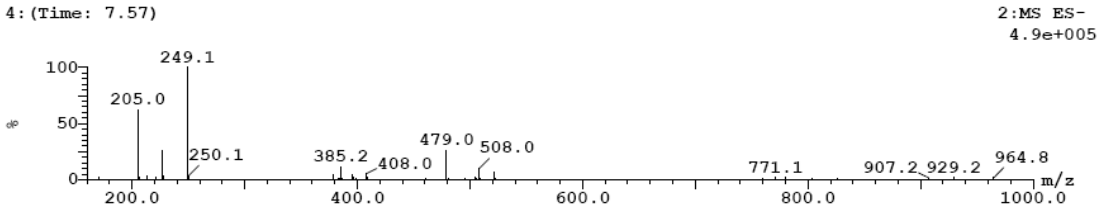
Peak ID	Compound	Time	Mass Found
2	Found	1.90	240.10



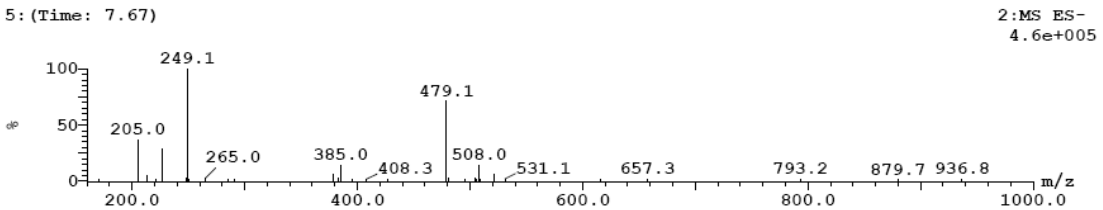
Peak ID	Compound	Time	Mass Found
3	Found	7.19	480.20



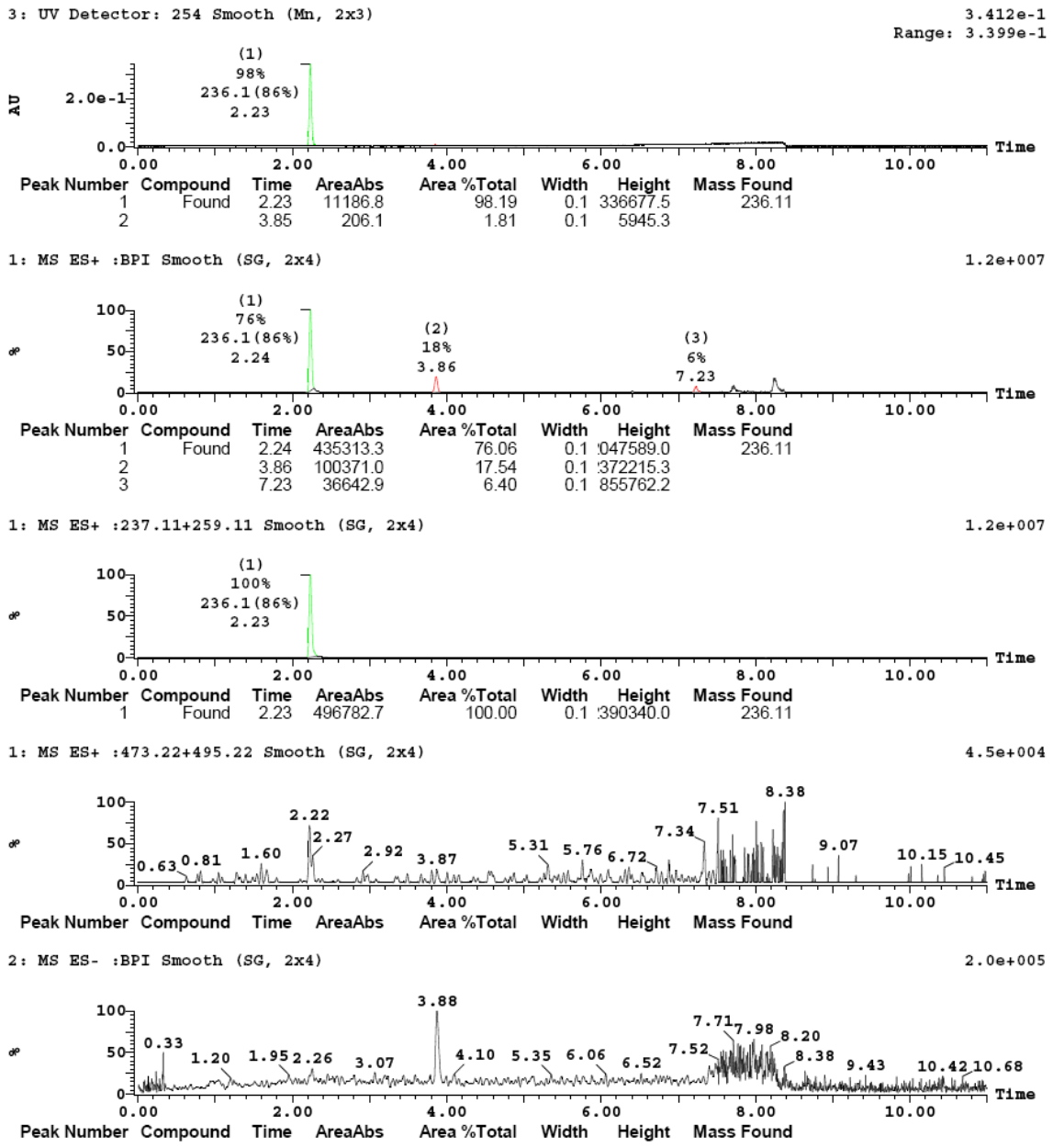
Peak ID	Compound	Time	Mass Found
4		7.57	

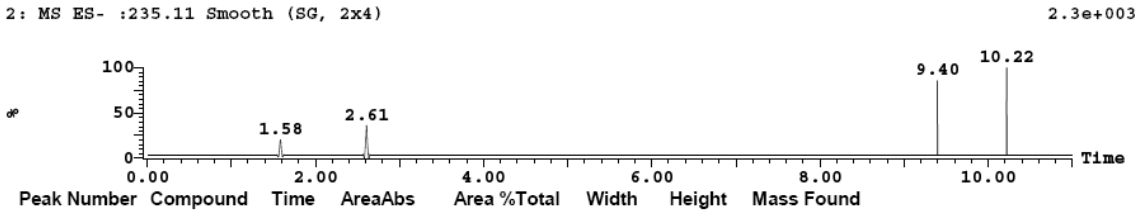


Peak ID	Compound	Time	Mass Found
5		7.67	

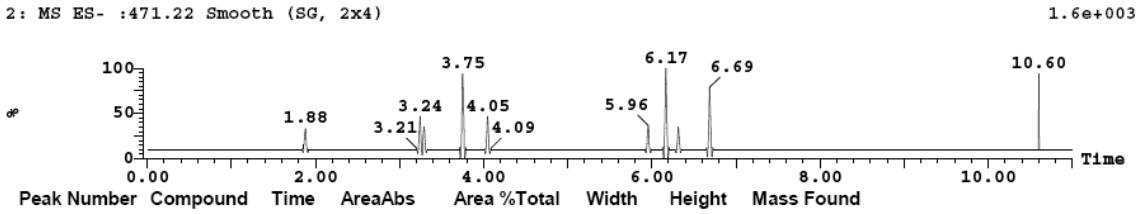


HT-LC-MS Spectrum (SOP 2200) of **4k**. UV purity: 98.2 %

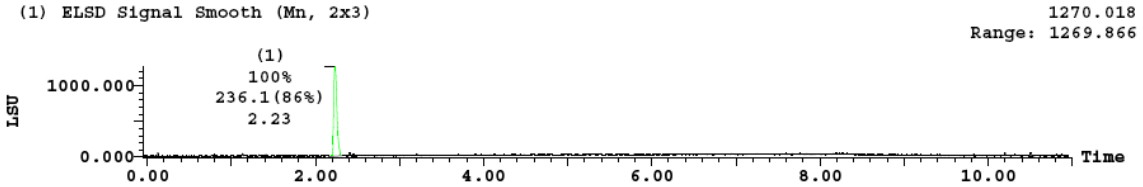




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

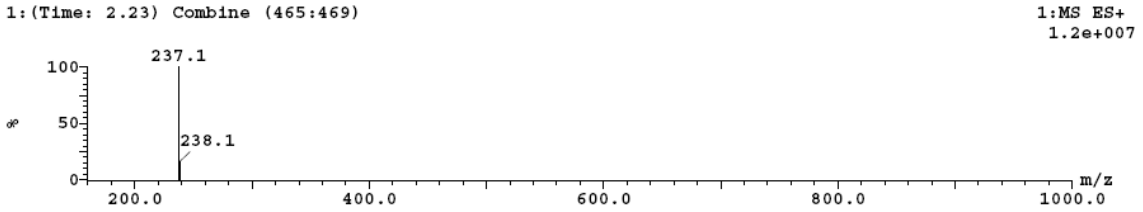


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

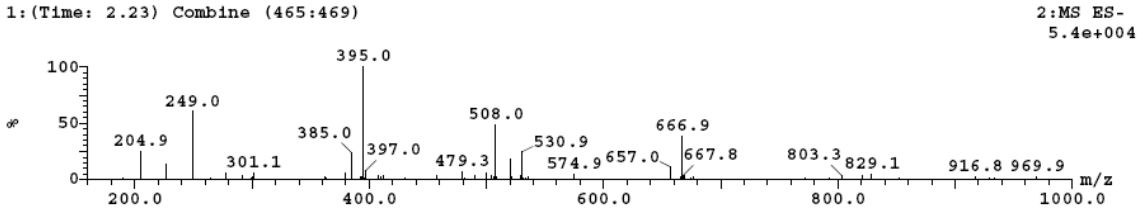


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	2.23	53790.0	100.00	256220.5	236.11

Peak ID	Compound	Time	Mass Found
1	Found	2.24	236.11



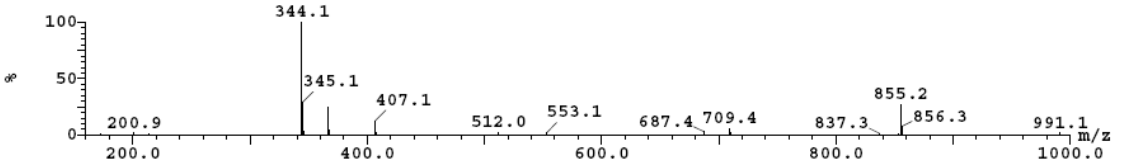
Peak ID	Compound	Time	Mass Found
1		2.24	



Peak ID	Compound	Time	Mass Found
2		3.86	

2:(Time: 3.86) Combine (806:810)

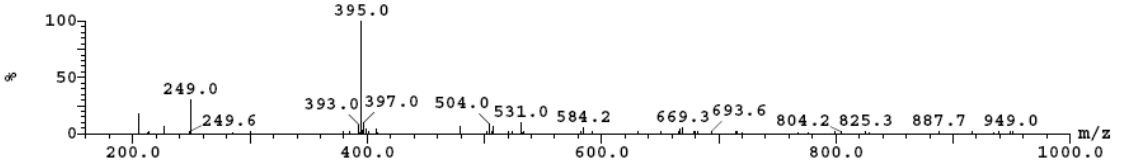
1:MS ES+
2.5e+006



Peak ID	Compound	Time	Mass Found
2		3.86	

2:(Time: 3.85) Combine (803:807)

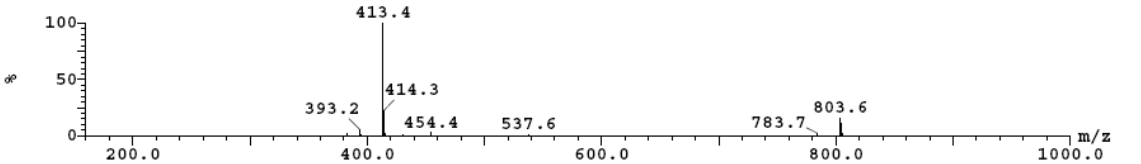
2:MS ES-
1.1e+005



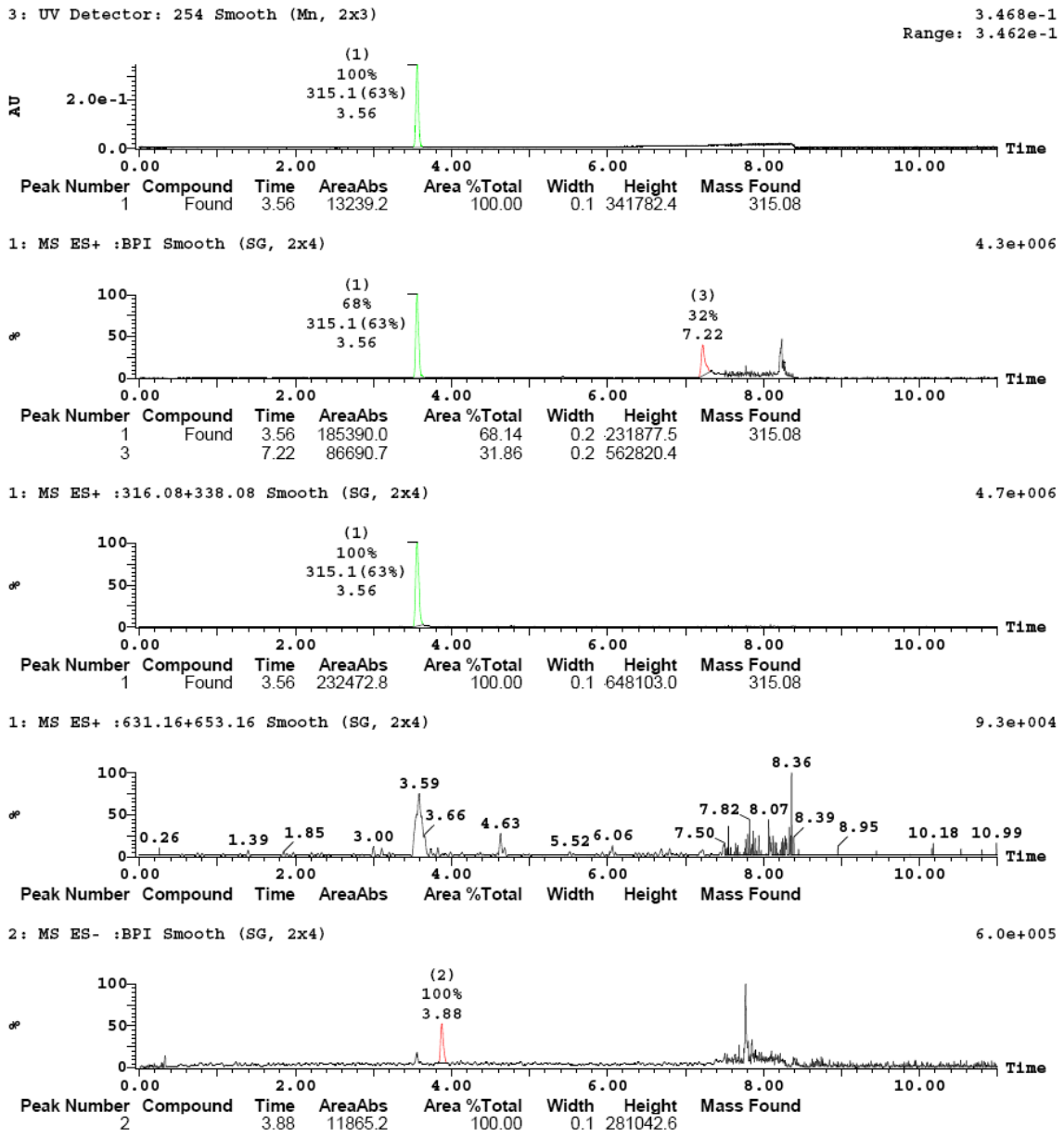
Peak ID	Compound	Time	Mass Found
3		7.23	

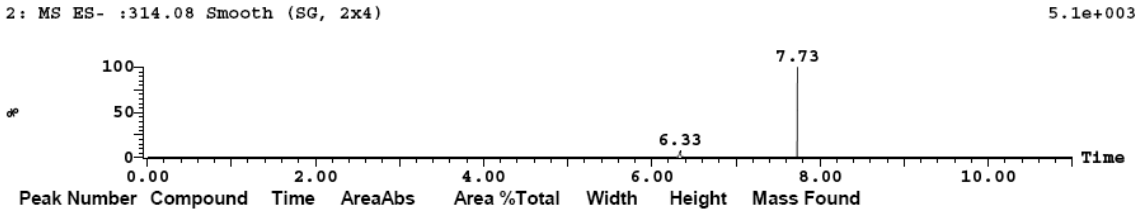
3:(Time: 7.23) Combine (1509:1513)

1:MS ES+
1.3e+006

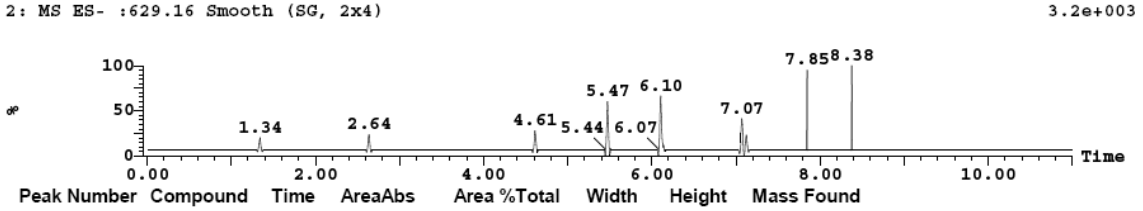


HT-LC-MS Spectrum (SOP 2200) of **4l**. UV purity: 100 %

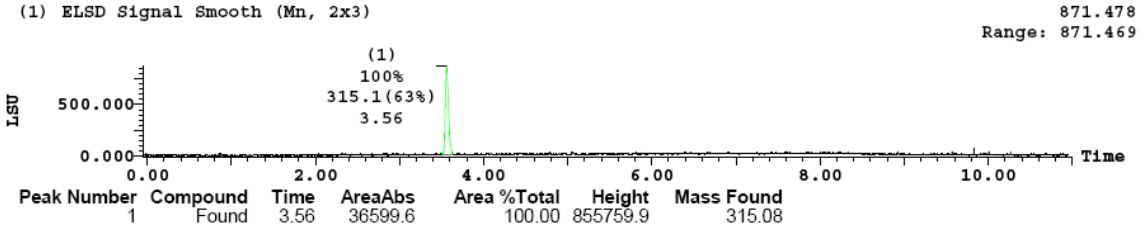




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

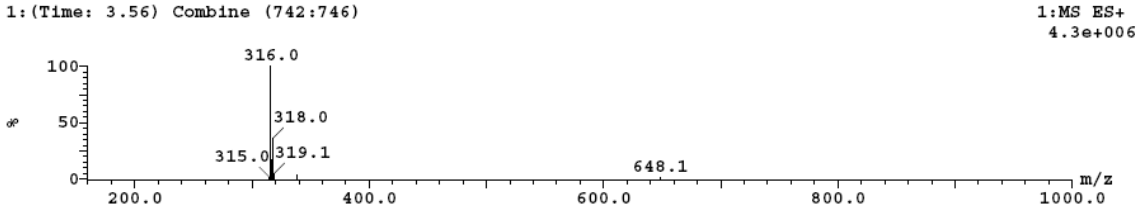


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

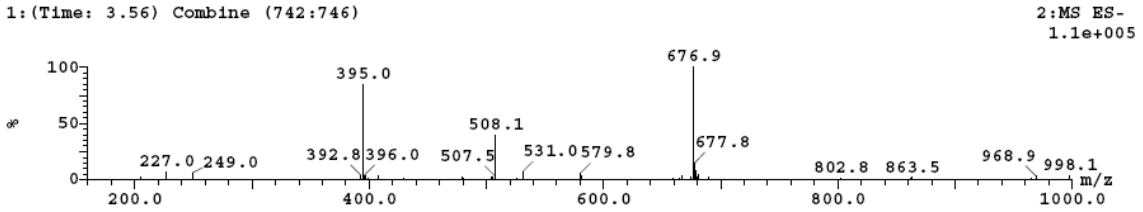


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	3.56	36599.6	100.00	855759.9	315.08

Peak ID	Compound	Time	Mass Found
1	Found	3.56	315.08

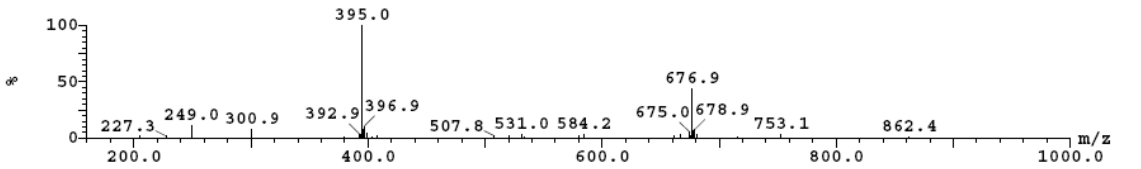


Peak ID	Compound	Time	Mass Found
1		3.56	



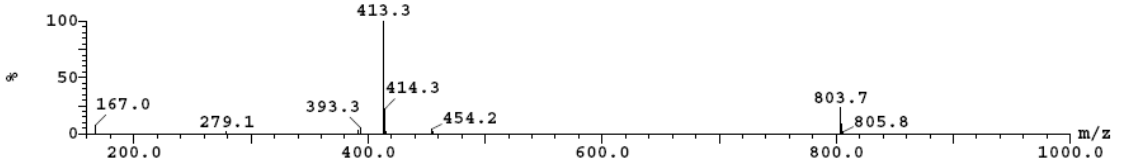
Peak ID	Compound	Time	Mass Found
2		3.88	

2:(Time: 3.88) Combine (808:812)

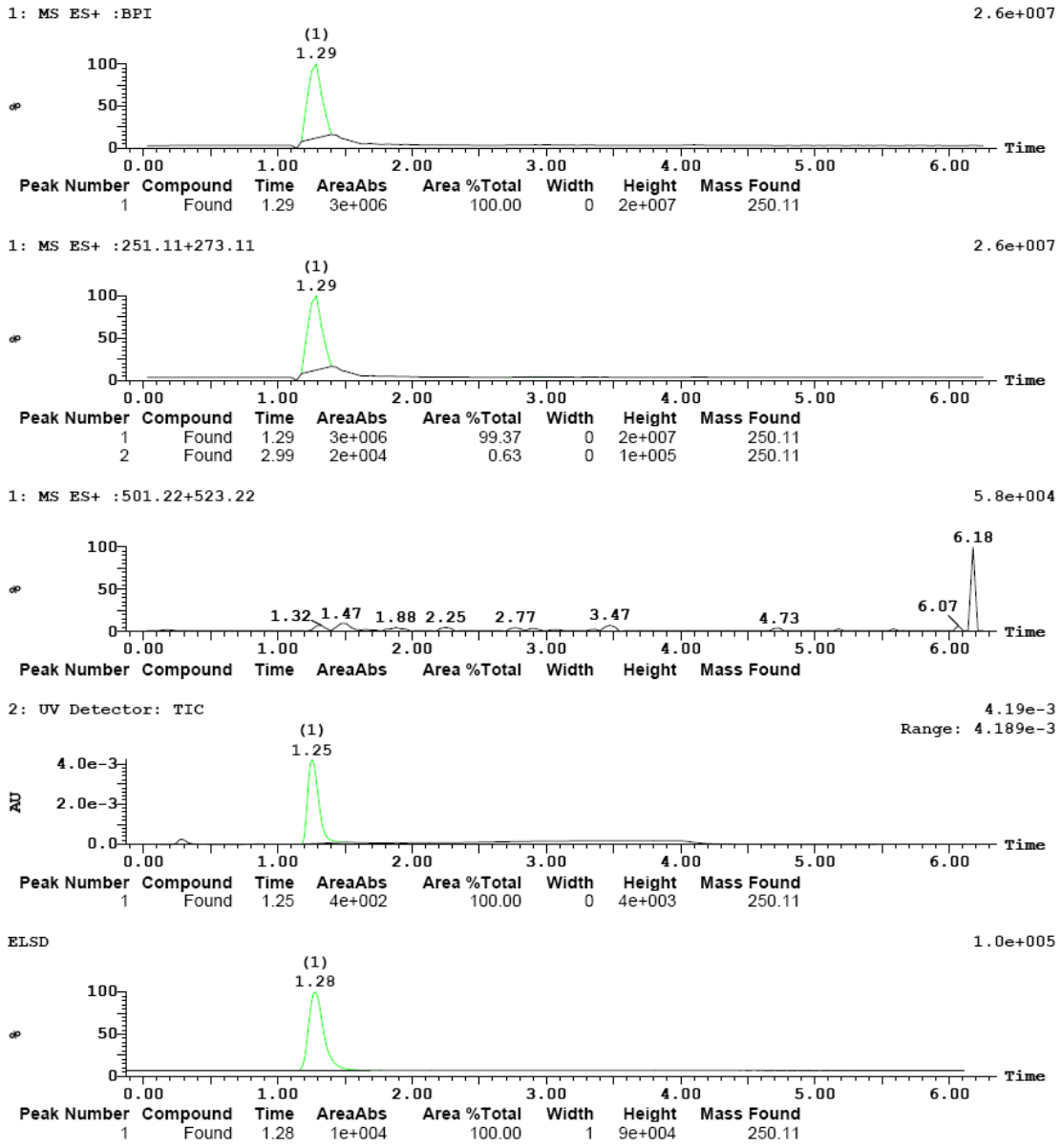


Peak ID	Compound	Time	Mass Found
3		7.22	

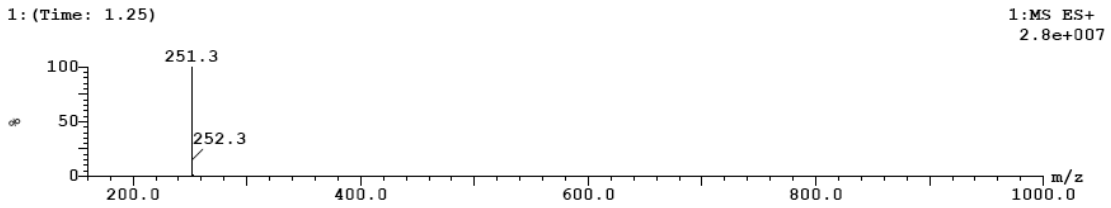
3:(Time: 7.22) Combine (1508:1512)



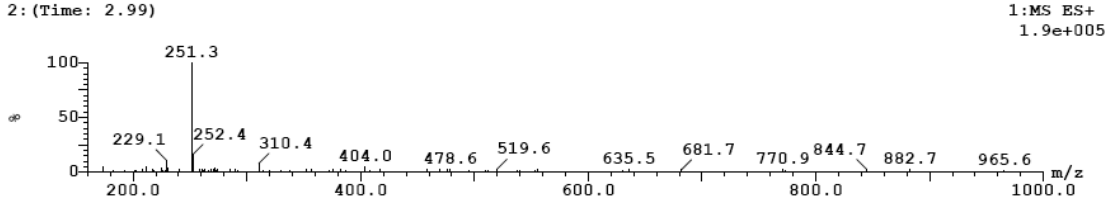
HT-LC-MS Spectrum (SOP 2222) of **4m**. UV purity: 100 %



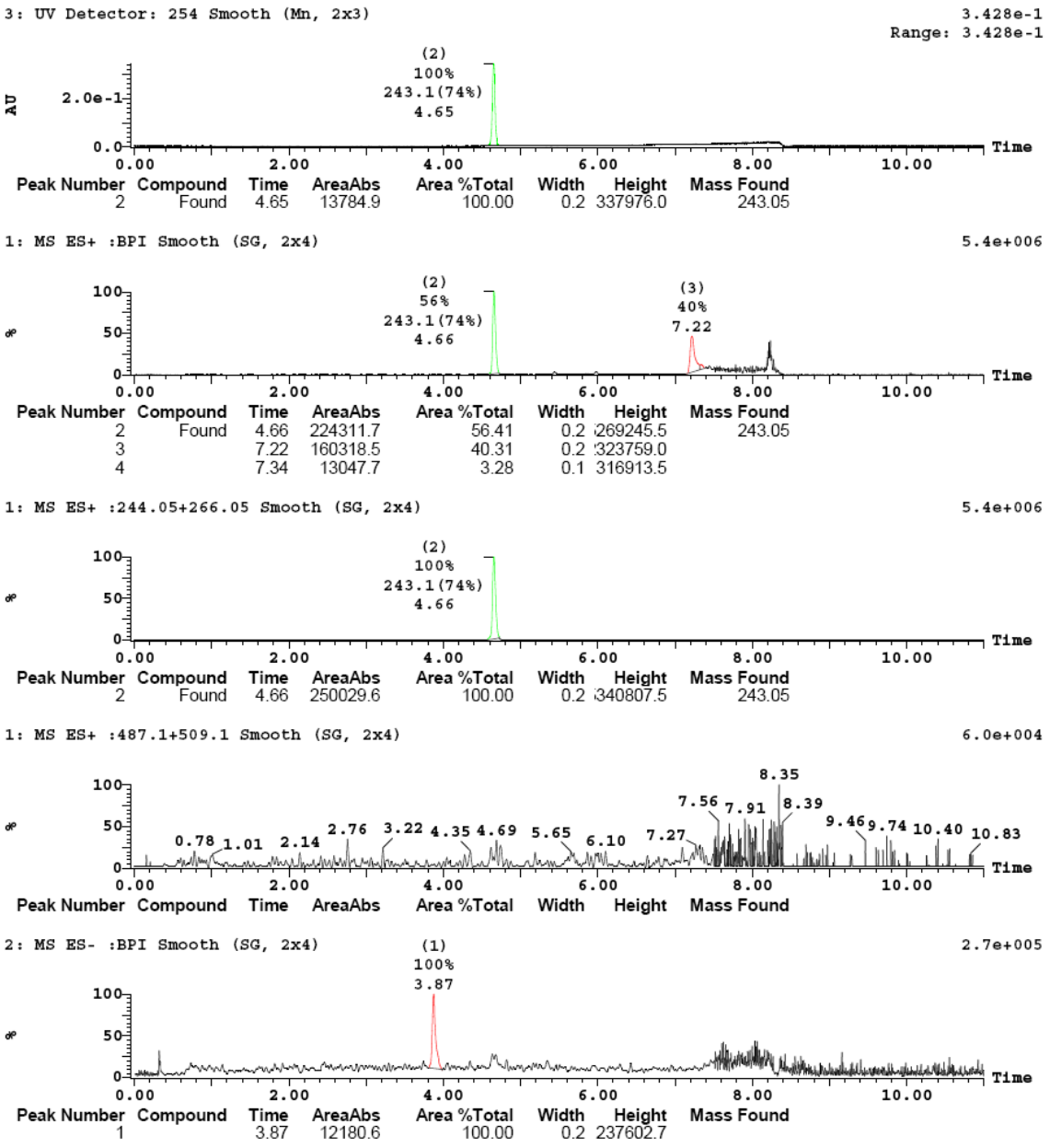
Peak ID	Compound	Time	Mass Found
1	Found	1.29	250.11

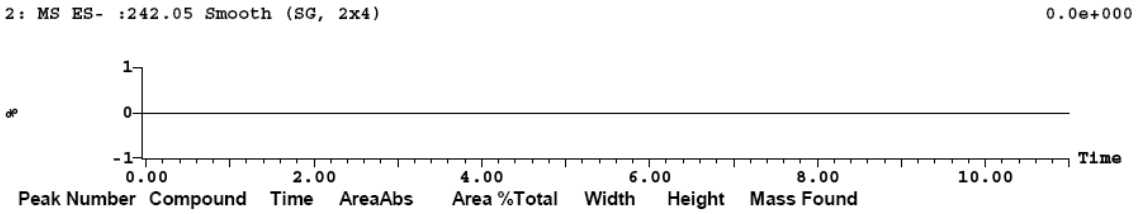


Peak ID	Compound	Time	Mass Found
2	Found	2.99	250.11

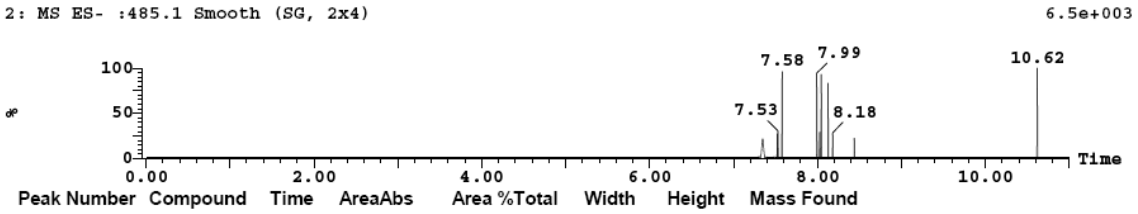


HT-LC-MS Spectrum (SOP 2200) of **4n**. UV purity: 100 %

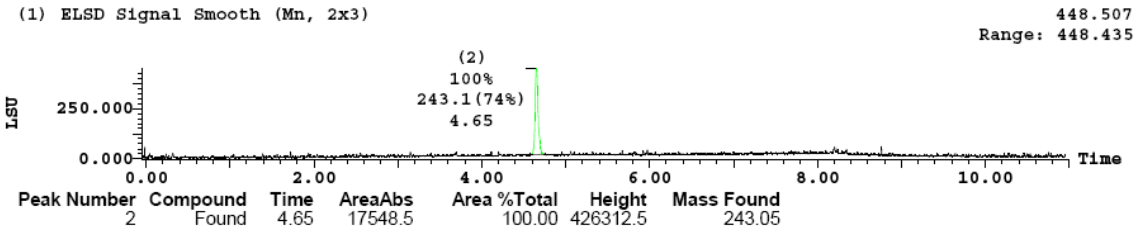




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

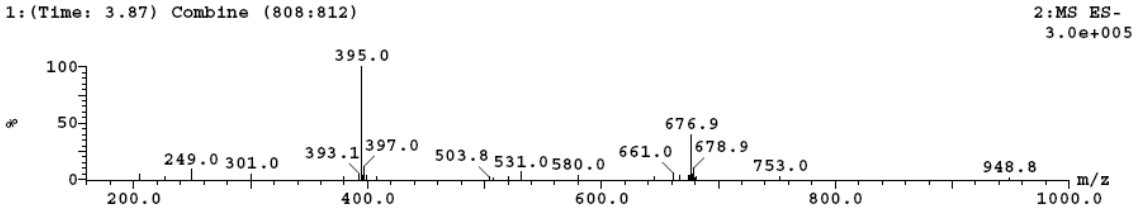


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

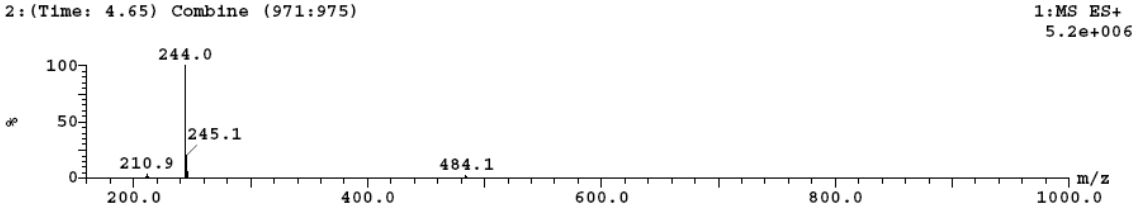


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
2	Found	4.65	17548.5	100.00	426312.5	243.05

Peak ID	Compound	Time	Mass Found
1		3.87	



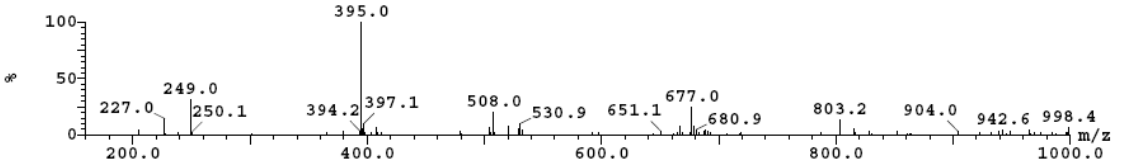
Peak ID	Compound	Time	Mass Found
2	Found	4.66	243.05



Peak ID	Compound	Time	Mass Found
2		4.66	

2:(Time: 4.65) Combine (970:974)

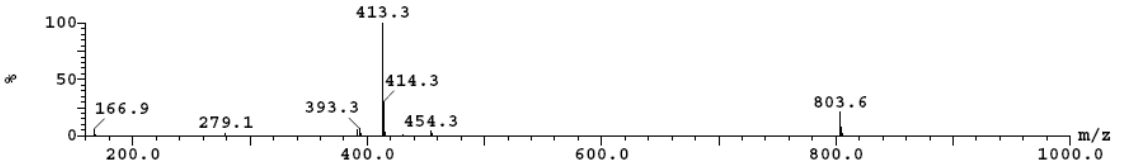
2:MS ES-
7.7e+004



Peak ID	Compound	Time	Mass Found
3		7.22	

3:(Time: 7.22) Combine (1507:1511)

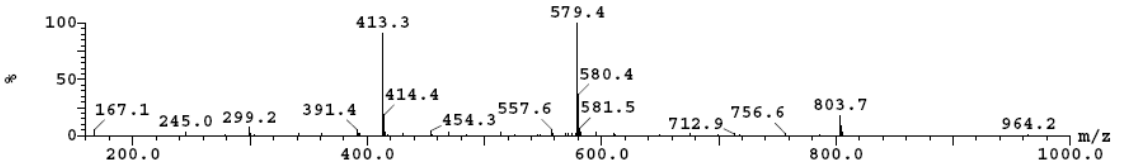
1:MS ES+
2.5e+006



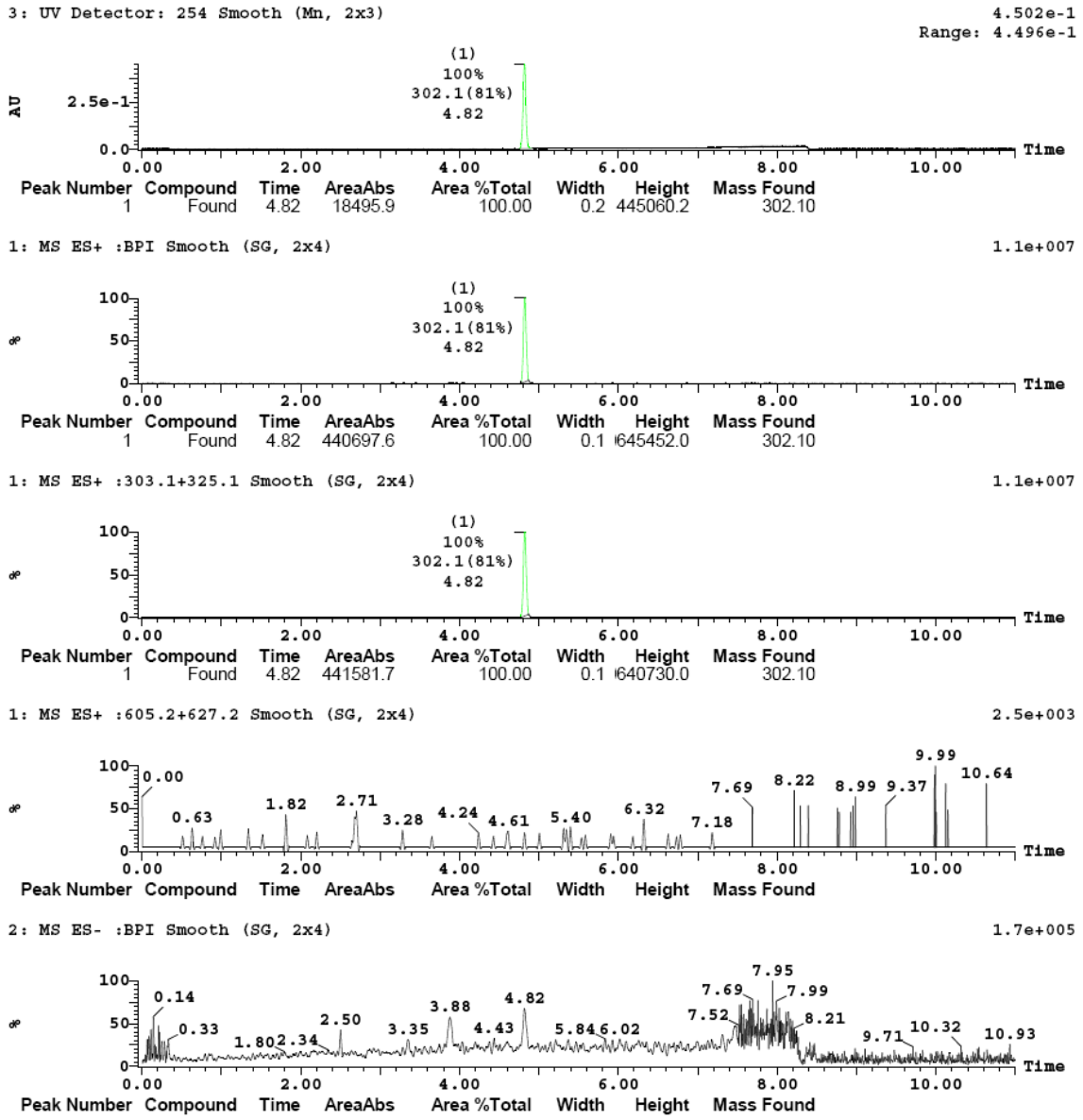
Peak ID	Compound	Time	Mass Found
4		7.34	

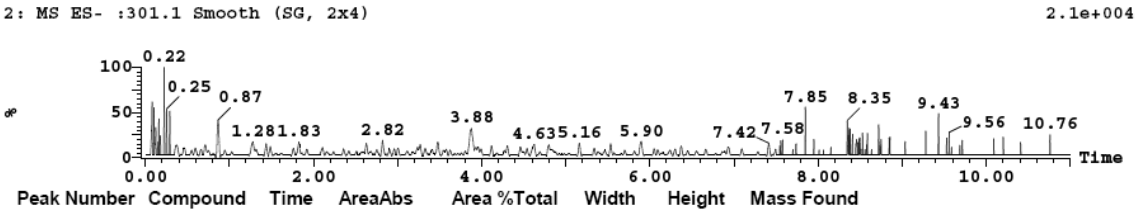
4:(Time: 7.34) Combine (1533:1537)

1:MS ES+
8.2e+005

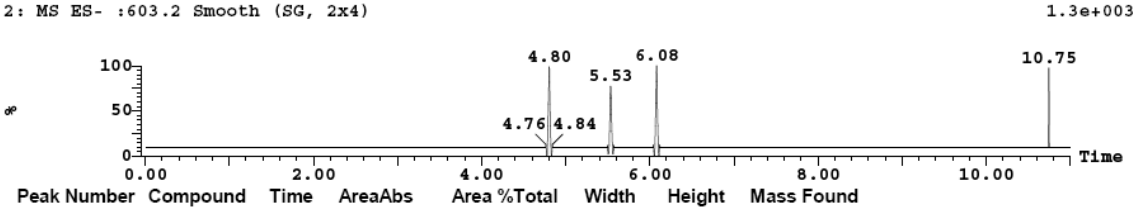


HT-LC-MS Spectrum (SOP 2200) of **4o**. UV purity: 100 %

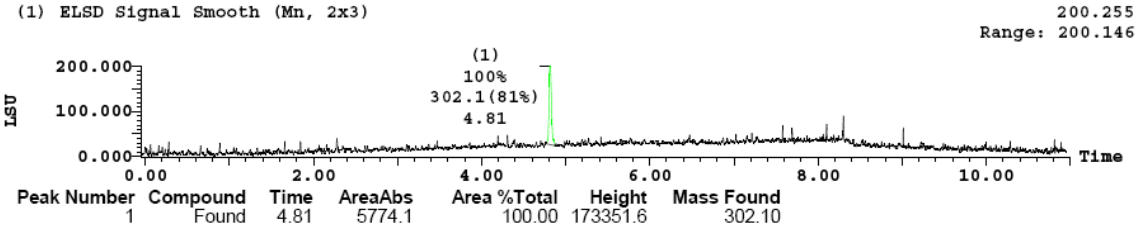




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

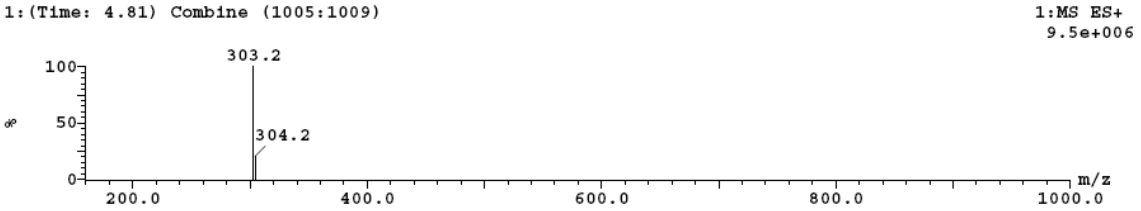


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

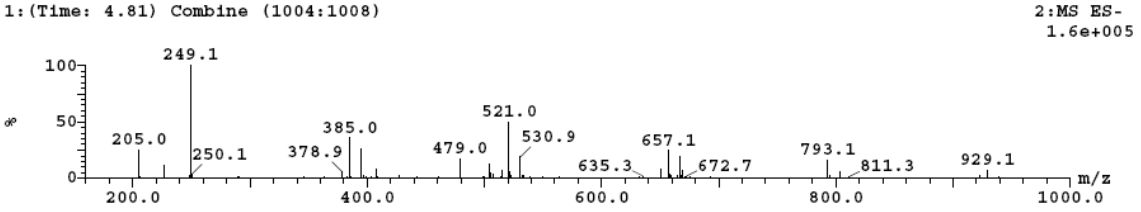


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	4.81	5774.1	100.00	173351.6	302.10

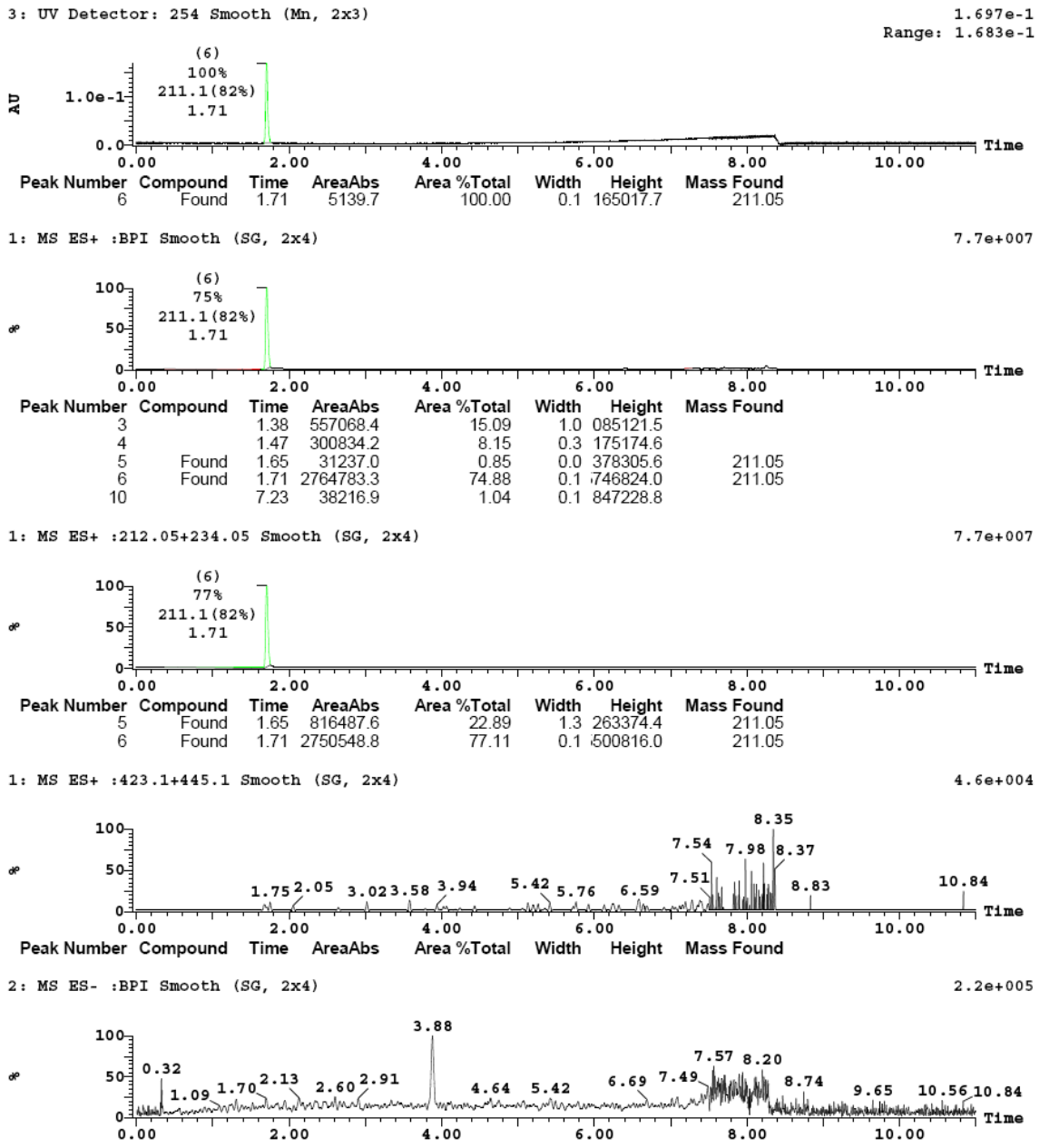
Peak ID	Compound	Time	Mass Found
1	Found	4.82	302.10



Peak ID	Compound	Time	Mass Found
1		4.82	

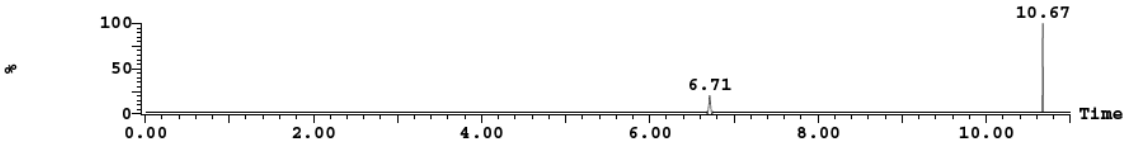


HT-LC-MS Spectrum (SOP 2200) of **4p**. UV purity: 100 %



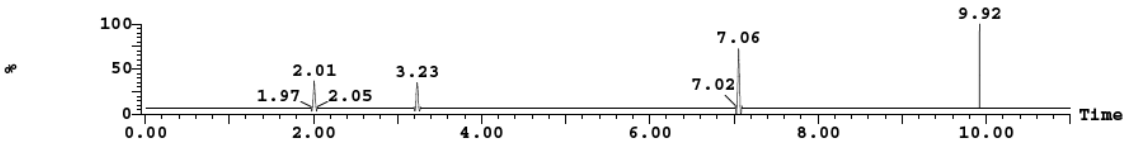
Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

2: MS ES- :210.05 Smooth (SG, 2x4) 2.0e+003



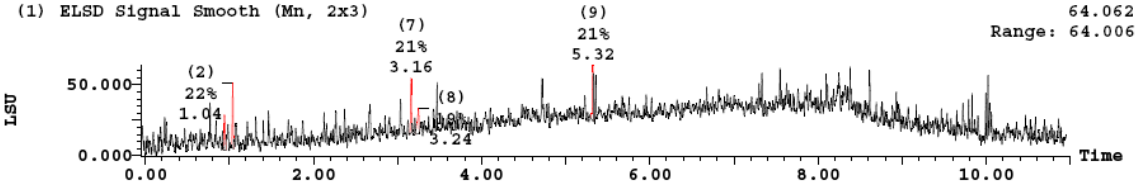
Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

2: MS ES- :421.1 Smooth (SG, 2x4) 1.6e+003



Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found

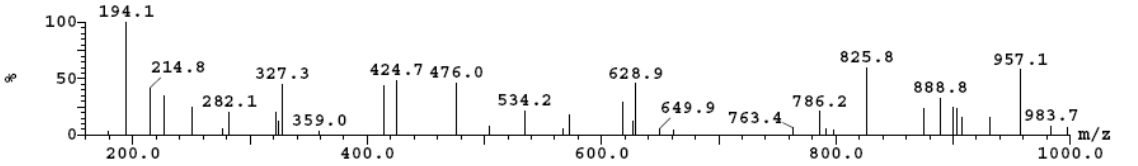
(1) ELSD Signal Smooth (Mn, 2x3) 64.062
Range: 64.006



Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1		0.94	371.8	16.90	25138.2	
2		1.04	487.7	22.17	46176.1	
7		3.16	466.2	21.19	39158.9	
8		3.25	417.1	18.96	17590.3	
9		5.32	457.5	20.79	39418.6	

Peak ID	Compound	Time	Mass Found
1		0.94	

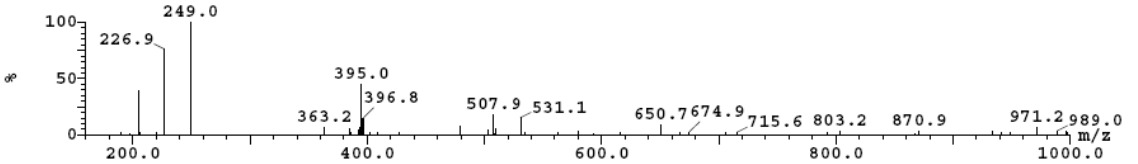
1:(Time: 0.94) Combine (196:200) 1:MS ES+
7.8e+003



Peak ID	Compound	Time	Mass Found
1		0.94	

1:(Time: 0.94) Combine (195:199)

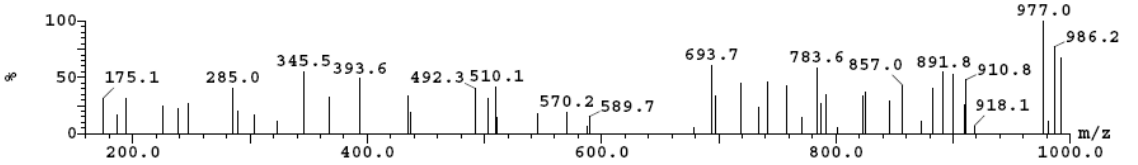
2:MS ES-
2.0e+004



Peak ID	Compound	Time	Mass Found
2		1.04	

2:(Time: 1.04) Combine (216:220)

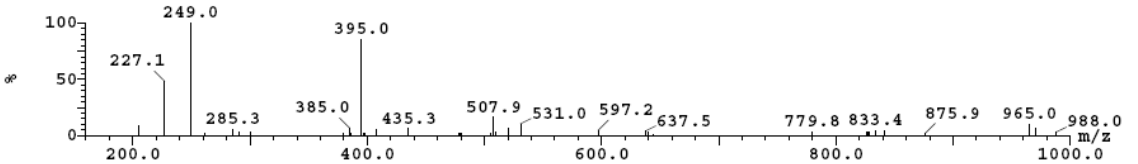
1:MS ES+
5.5e+003



Peak ID	Compound	Time	Mass Found
2		1.04	

2:(Time: 1.04) Combine (215:220)

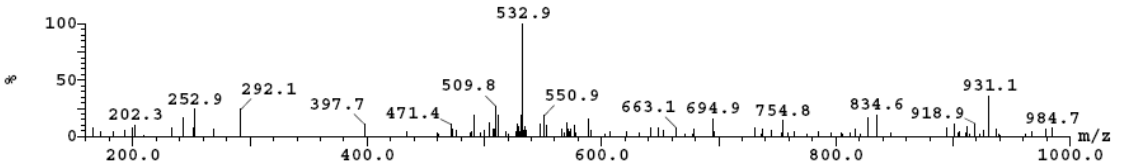
2:MS ES-
2.3e+004



Peak ID	Compound	Time	Mass Found
3		1.38	

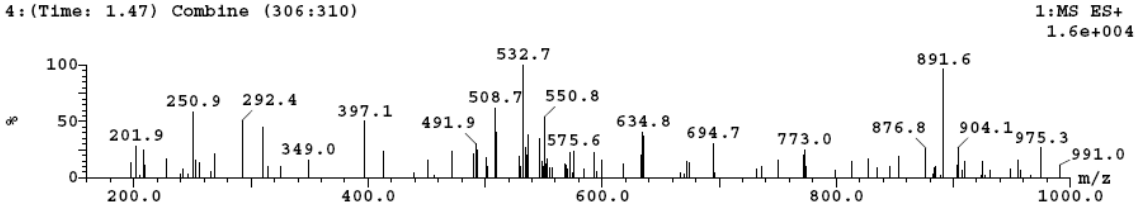
3:(Time: 1.38) Combine (286:290)

1:MS ES+
3.5e+004



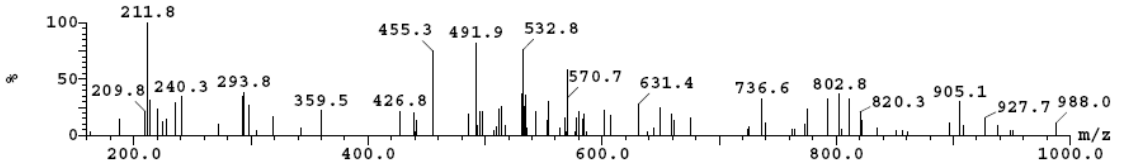
Peak ID	Compound	Time	Mass Found
4		1.47	

4:(Time: 1.47) Combine (306:310)



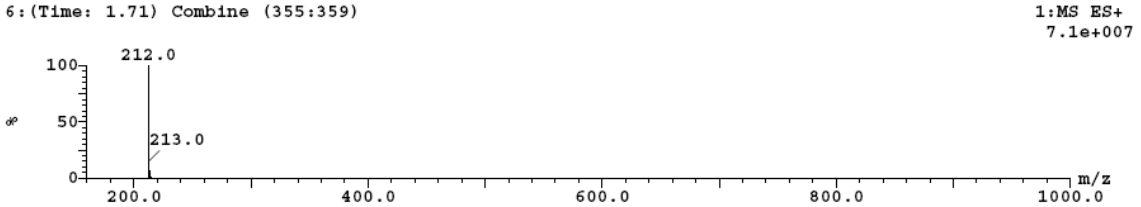
Peak ID	Compound	Time	Mass Found
5	Found	1.65	211.05

5:(Time: 1.65) Combine (343:347)



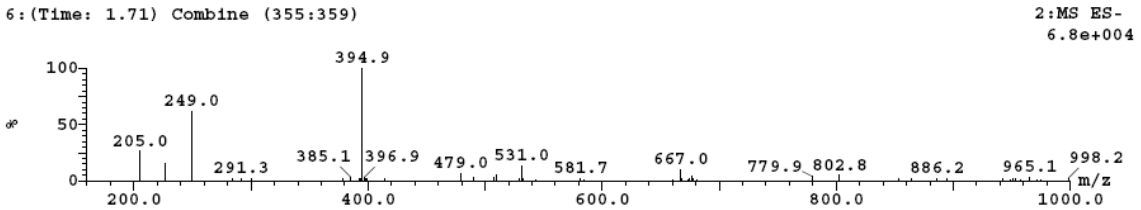
Peak ID	Compound	Time	Mass Found
6	Found	1.71	211.05

6:(Time: 1.71) Combine (355:359)



Peak ID	Compound	Time	Mass Found
6		1.71	

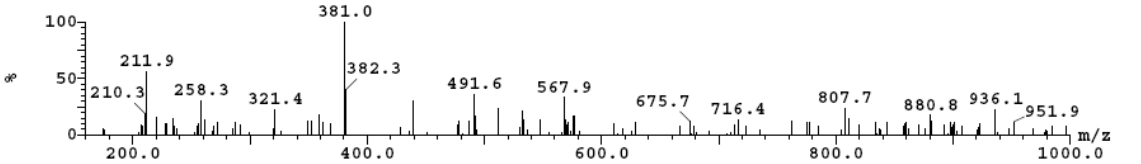
6:(Time: 1.71) Combine (355:359)



Peak ID	Compound	Time	Mass Found
7		3.16	

7:(Time: 3.16) Combine (659:663)

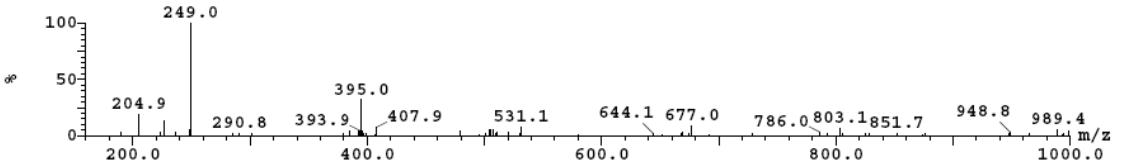
1:MS ES+
2.7e+004



Peak ID	Compound	Time	Mass Found
7		3.16	

7:(Time: 3.16) Combine (659:663)

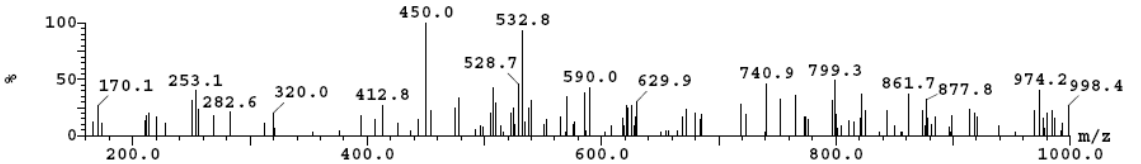
2:MS ES-
5.3e+004



Peak ID	Compound	Time	Mass Found
8		3.25	

8:(Time: 3.25) Combine (677:681)

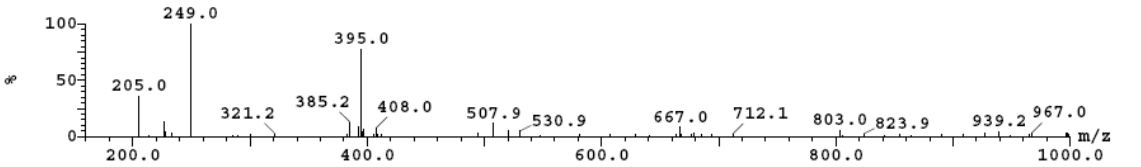
1:MS ES+
1.0e+004

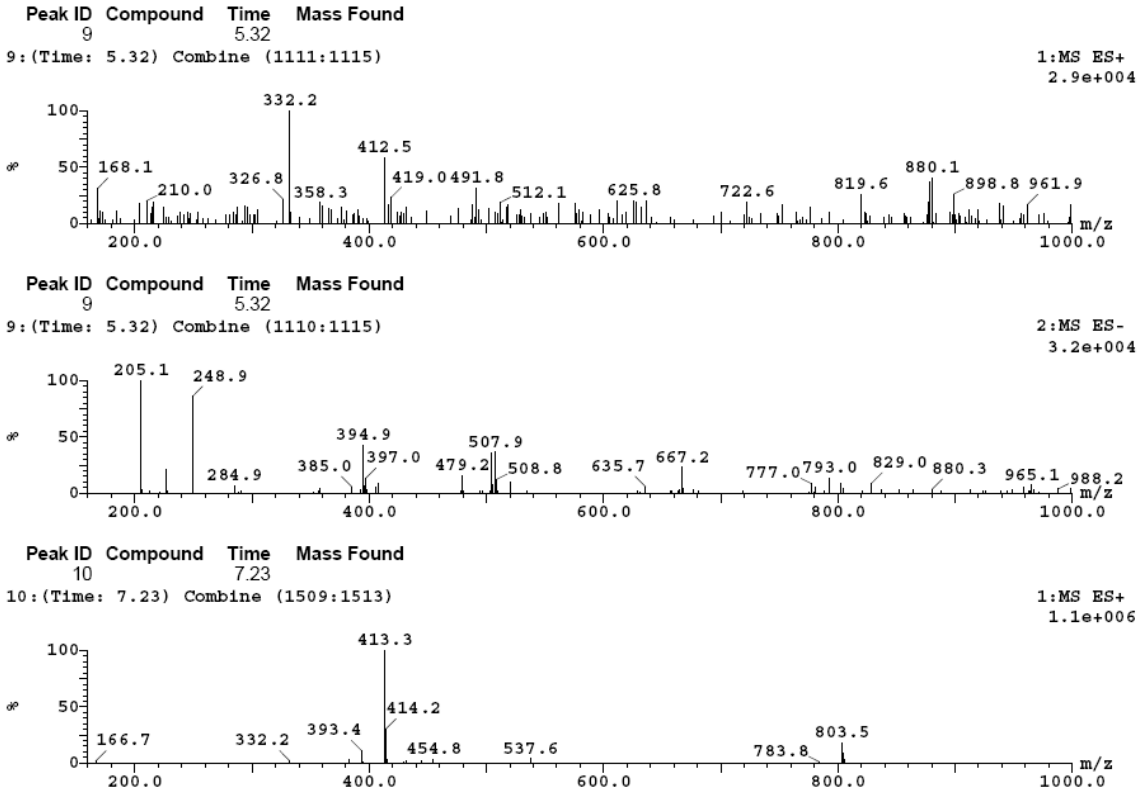


Peak ID	Compound	Time	Mass Found
8		3.25	

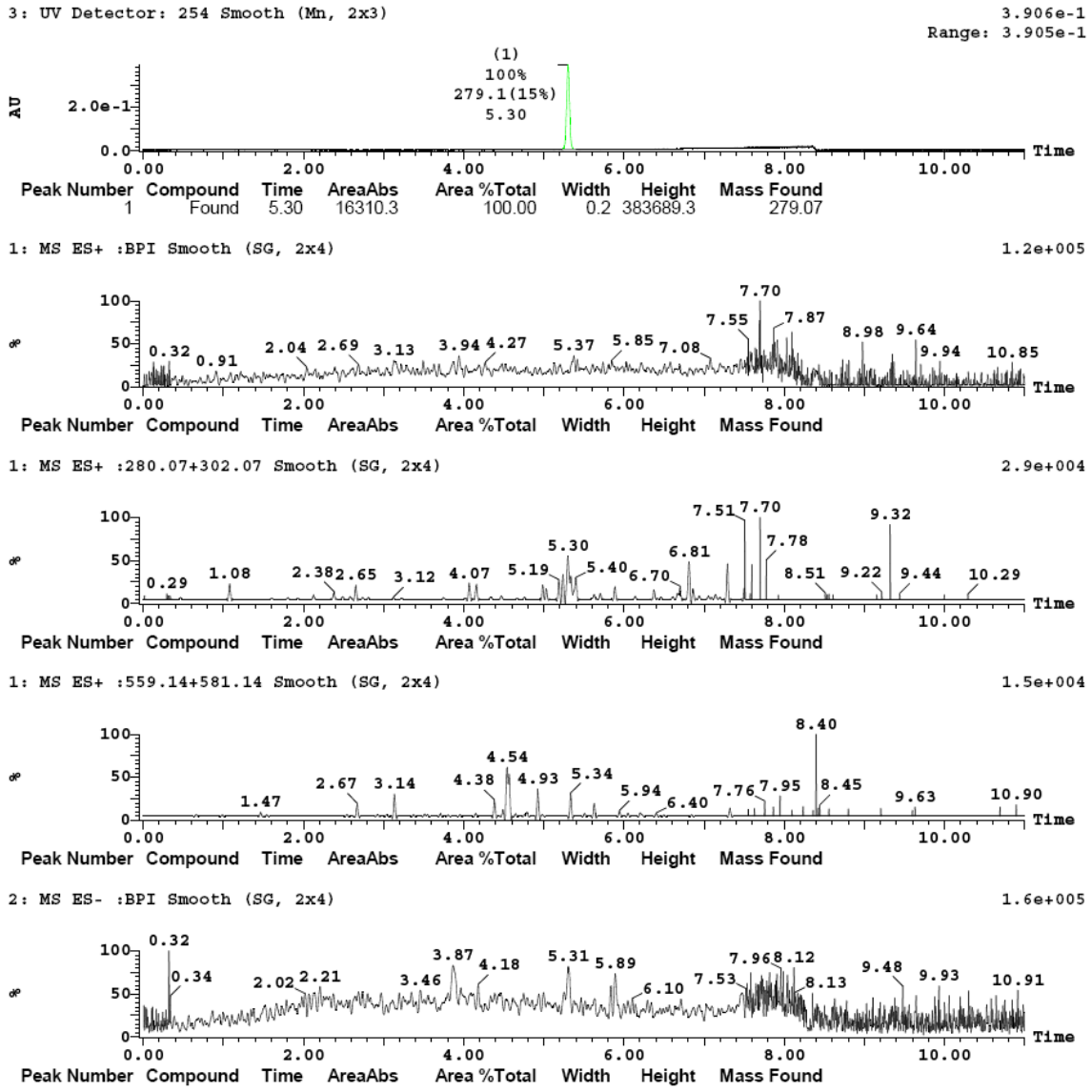
8:(Time: 3.25) Combine (676:681)

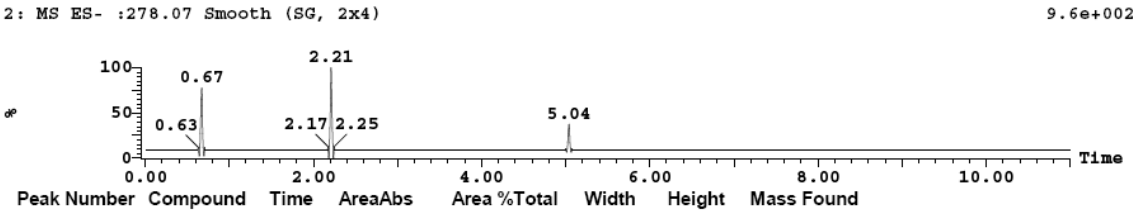
2:MS ES-
4.2e+004



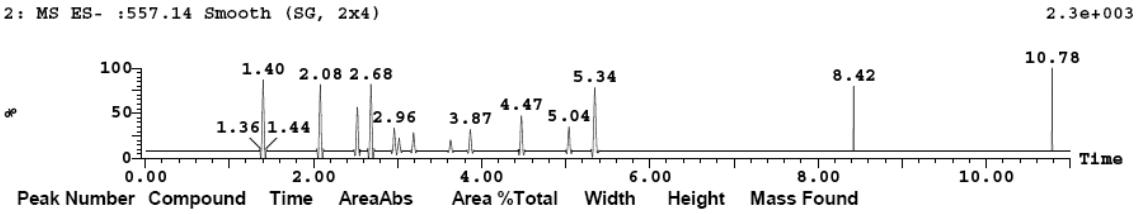

Peak ID Compound Time Mass Found
9 5.32
9:(Time: 5.32) Combine (1111:1115)
1:MS ES+
2.9e+004
100
50
0
%
332.2
412.5
168.1
210.0
326.8
358.3
419.0
491.8
512.1
625.8
722.6
819.6
880.1
898.8
961.9
200.0
400.0
600.0
800.0
1000.0
m/z
Peak ID Compound Time Mass Found
9 5.32
9:(Time: 5.32) Combine (1110:1115)
2:MS ES-
3.2e+004
205.1
248.9
394.9
507.9
284.9
385.0
397.0
479.2
508.8
635.7
667.2
777.0
793.0
829.0
880.3
965.1
988.2
Peak ID Compound Time Mass Found
10 7.23
10:(Time: 7.23) Combine (1509:1513)
1:MS ES+
1.1e+006
413.3
414.2
393.4
166.7
332.2
454.8
537.6
783.8
803.5

HT-LC-MS Spectrum (SOP 2200) of **4q**. UV purity: 100 %

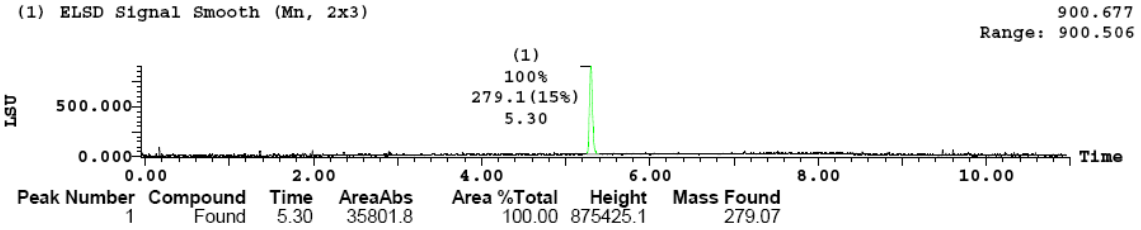




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

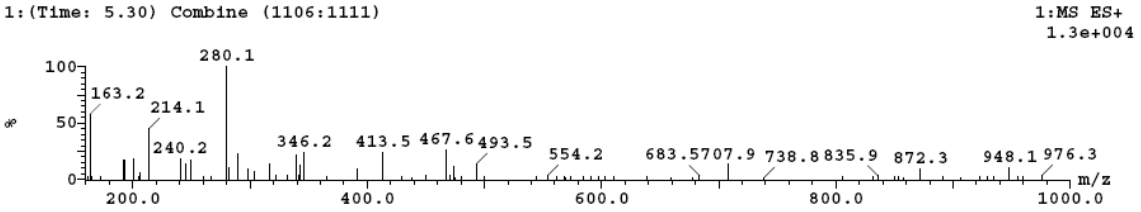


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

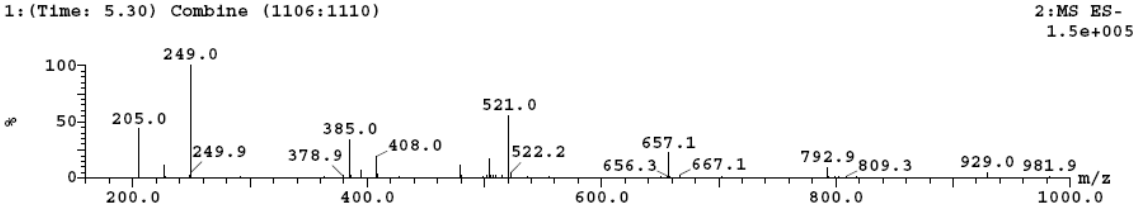


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	5.30	35801.8	100.00	875425.1	279.07

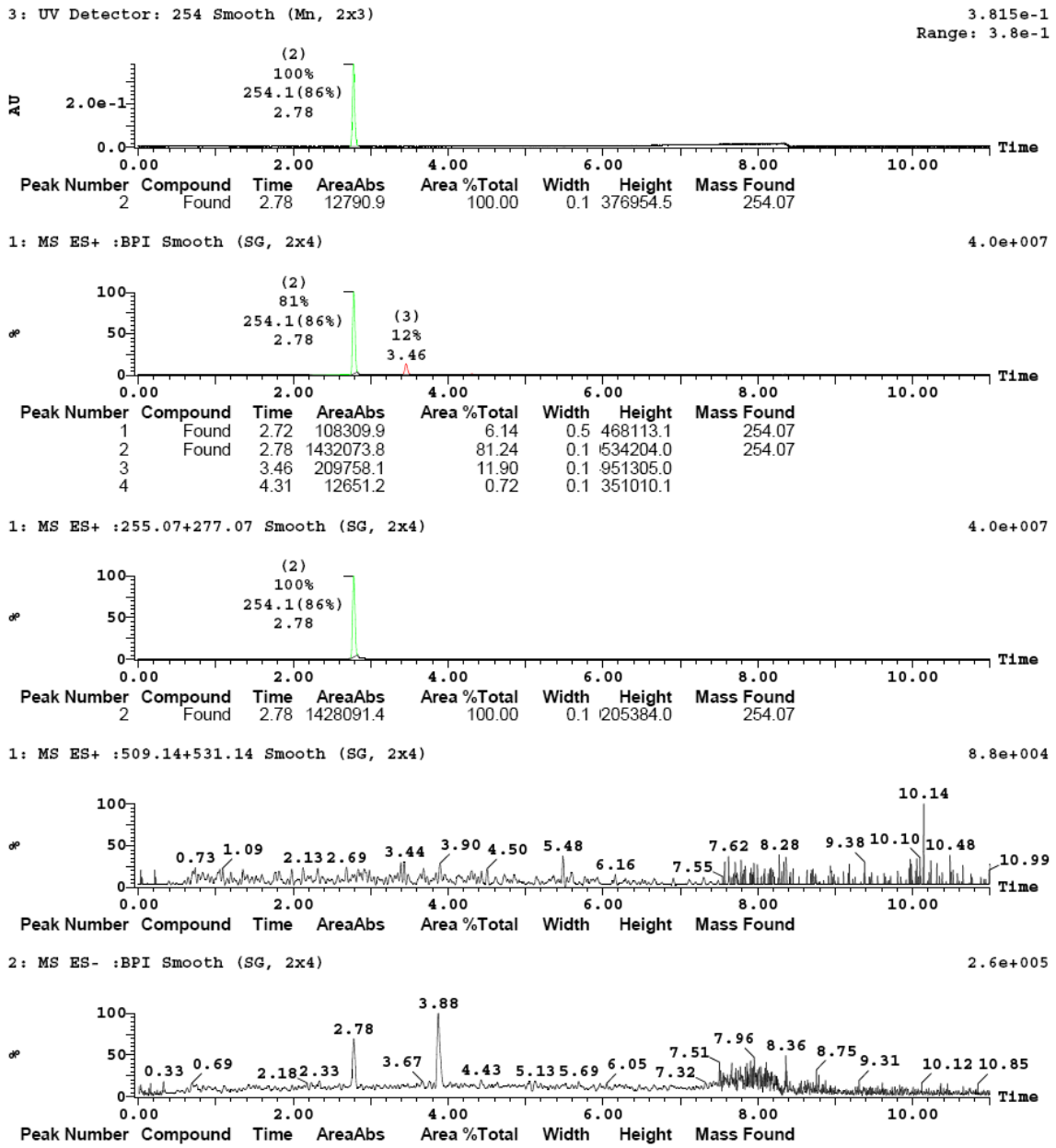
Peak ID	Compound	Time	Mass Found
1	Found	5.30	279.07

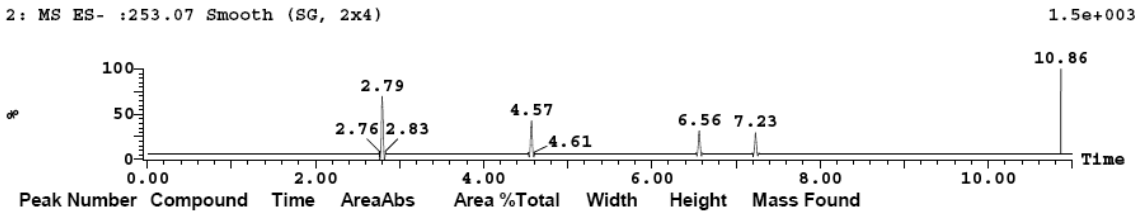


Peak ID	Compound	Time	Mass Found
1		5.30	

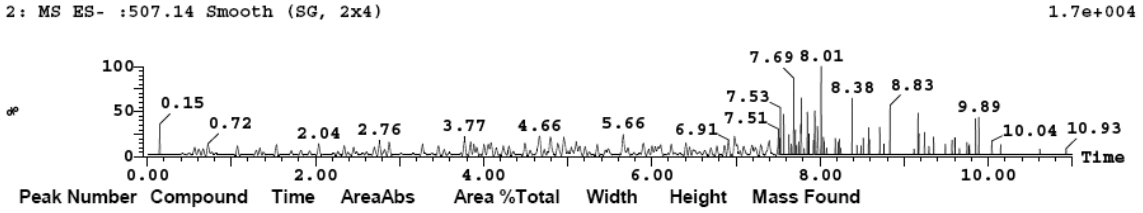


HT-LC-MS Spectrum (SOP 2200) of **4r**. UV purity: 100 %

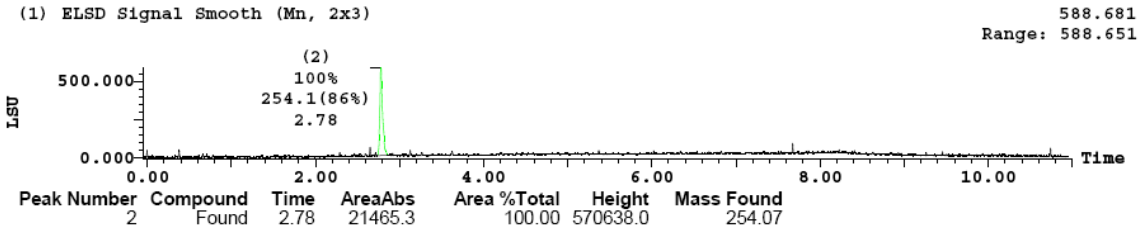




Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found

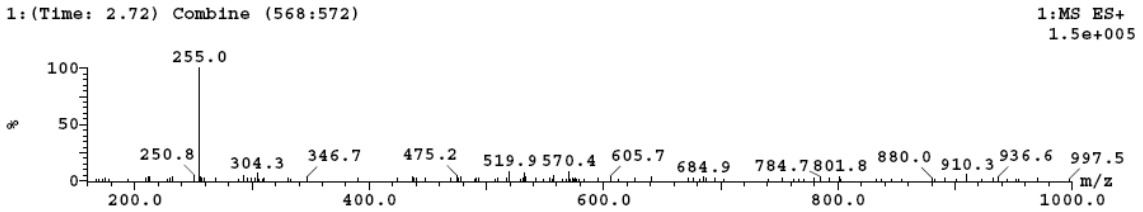


Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found

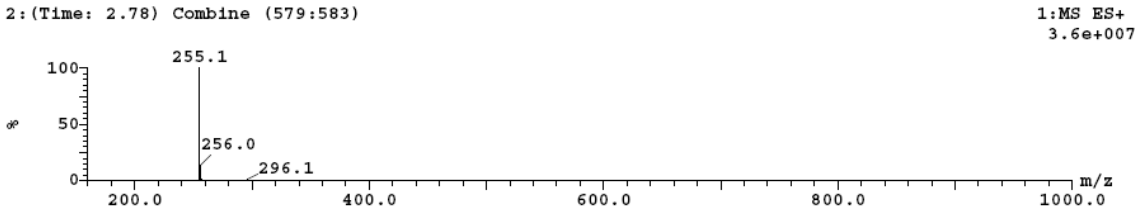


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
2	Found	2.78	21465.3	100.00	570638.0	254.07

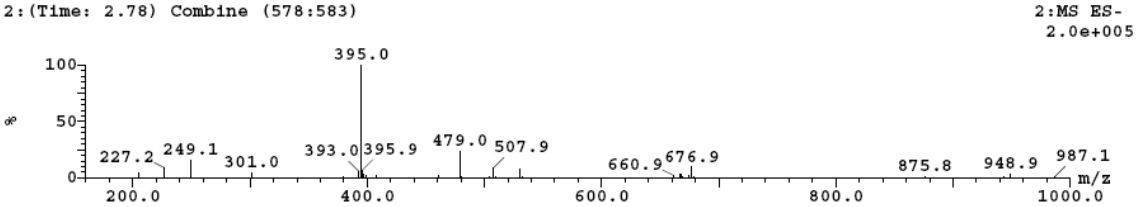
Peak ID	Compound	Time	Mass Found
1	Found	2.72	254.07



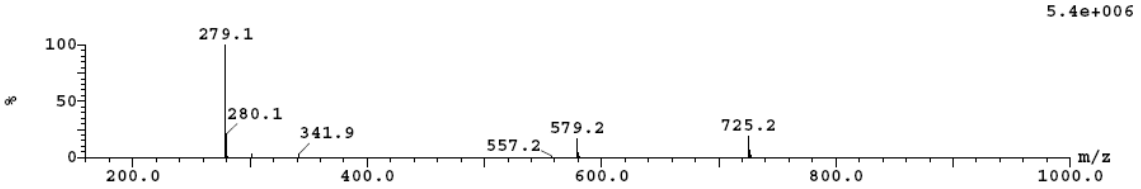
Peak ID	Compound	Time	Mass Found
2	Found	2.78	254.07



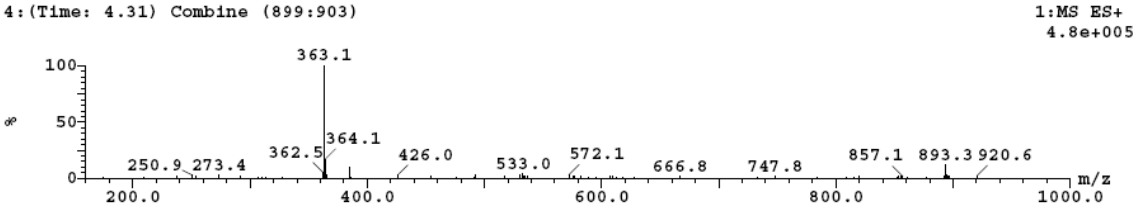
Peak ID	Compound	Time	Mass Found
2		2.78	



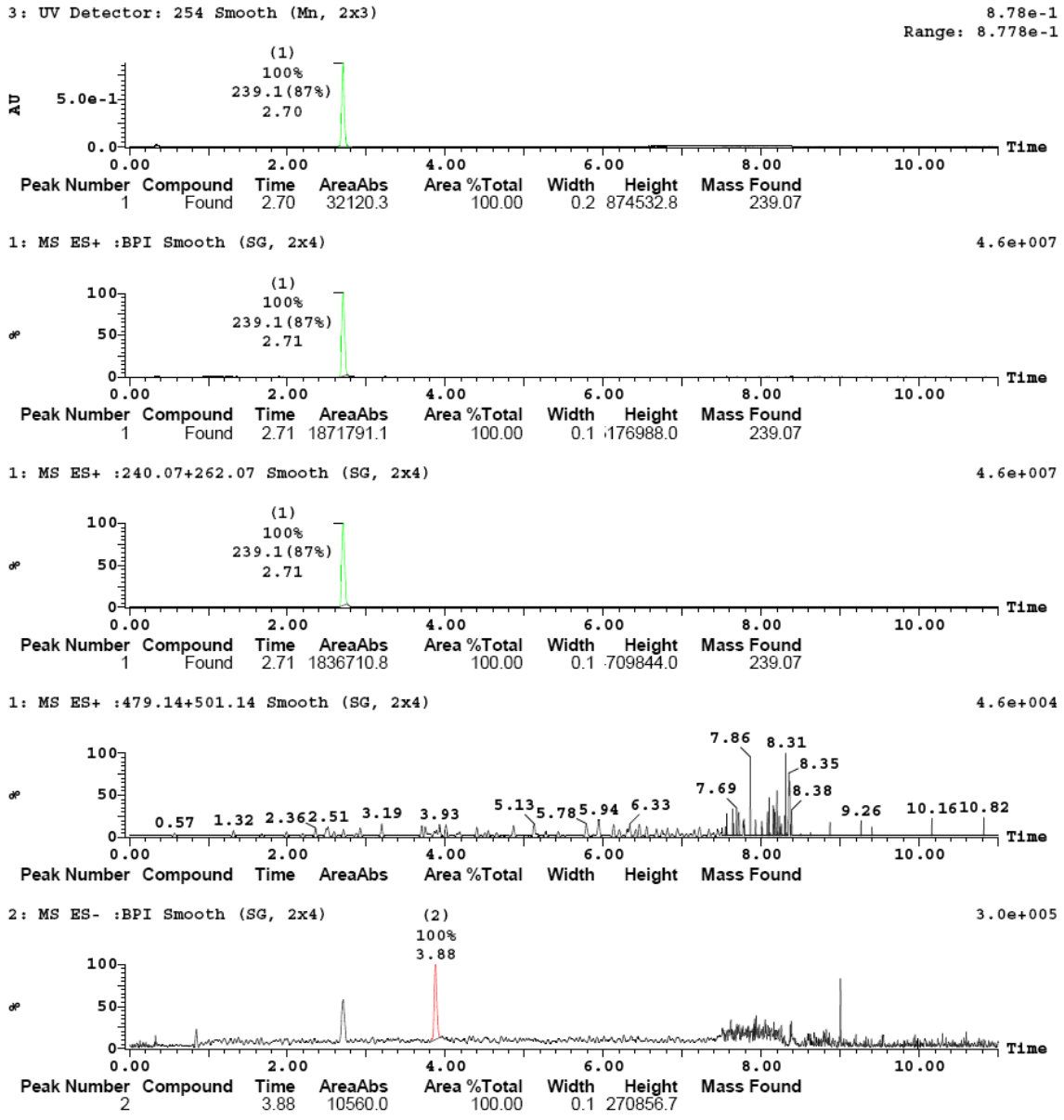
Peak ID	Compound	Time	Mass Found
3		3.46	

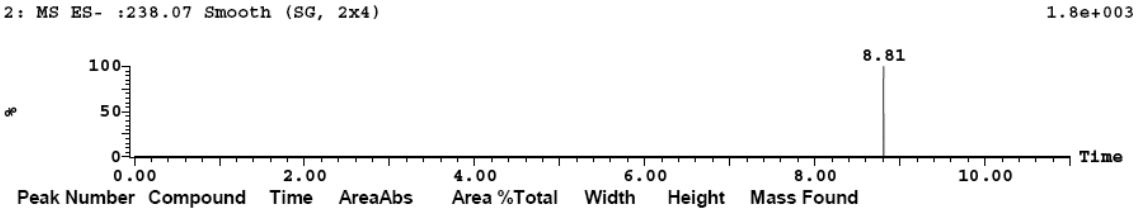


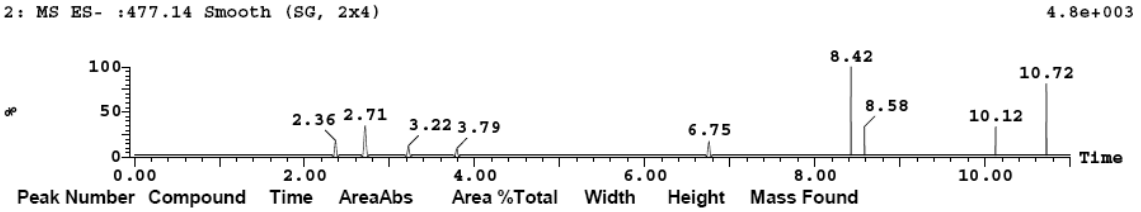
Peak ID	Compound	Time	Mass Found
4		4.31	

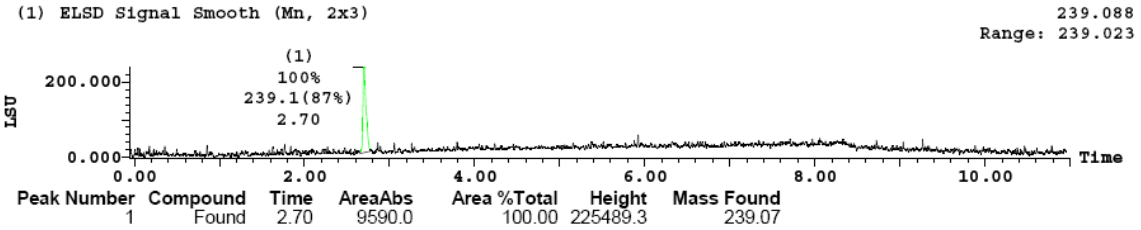


HP-LC-MS Spectrum (SOP 2200) of **4s**. UV purity: 100 %

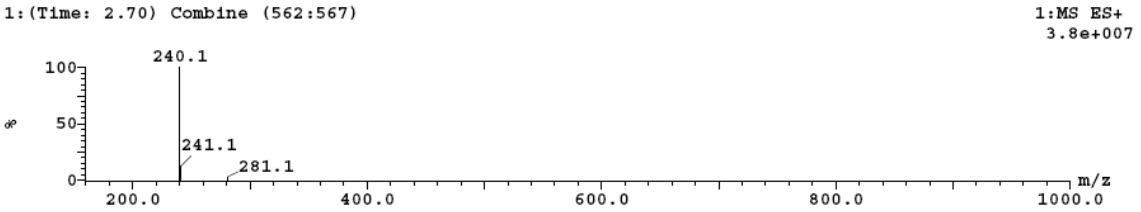




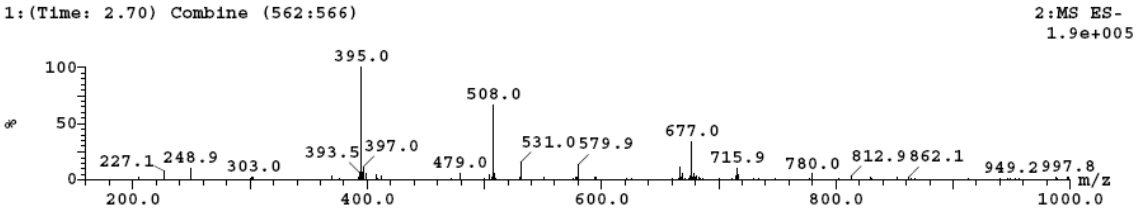




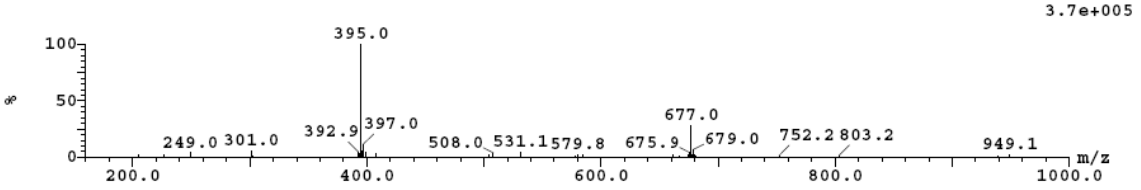
Peak ID Compound Time Mass Found
1 Found 2.71 239.07



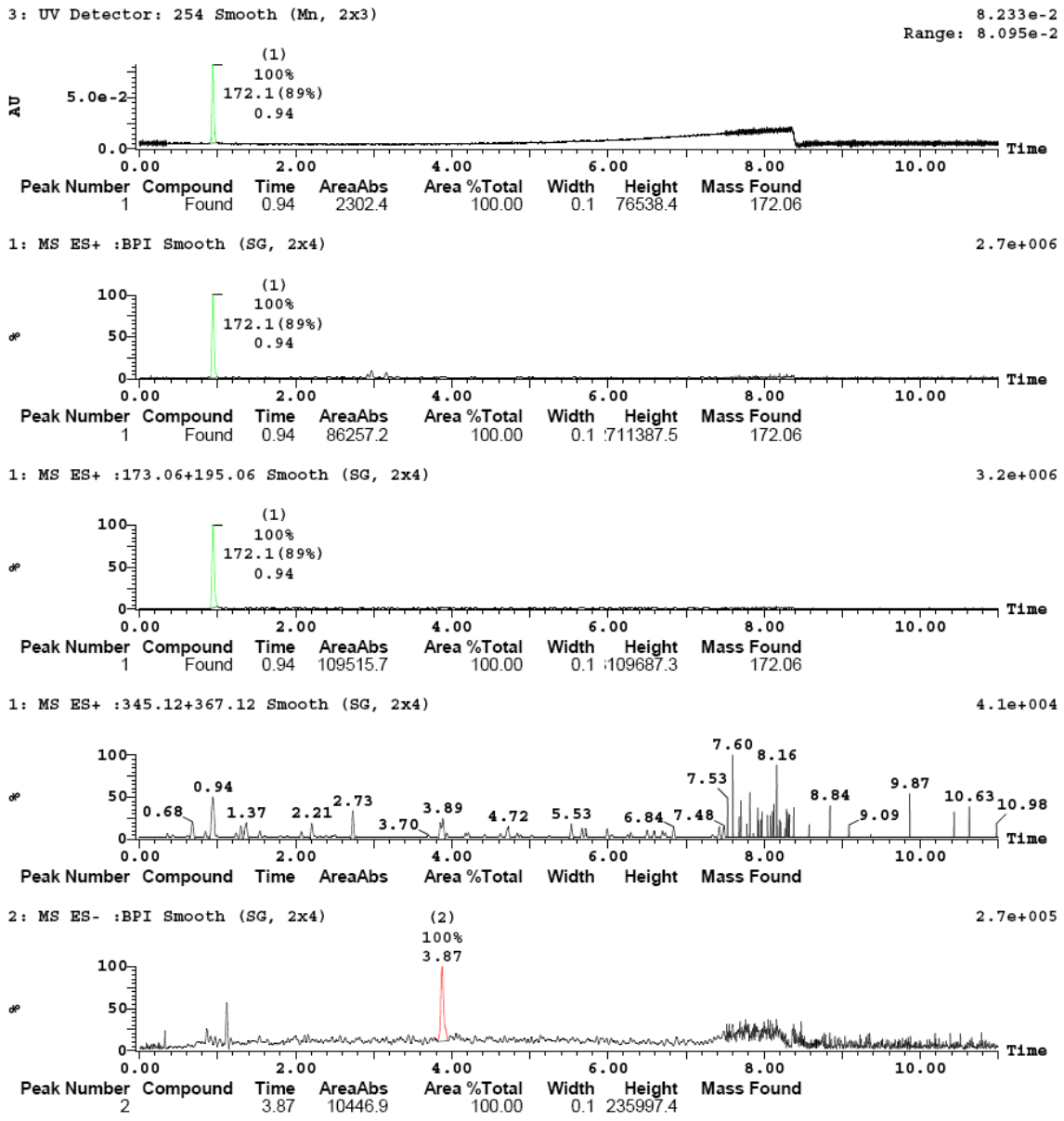
Peak ID Compound Time Mass Found
1 2.71

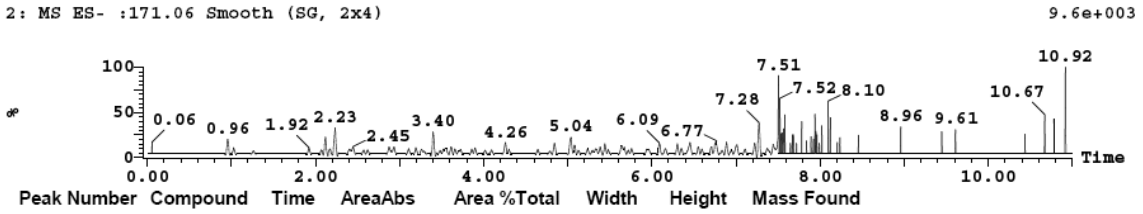


Peak ID Compound Time Mass Found
2 3.88

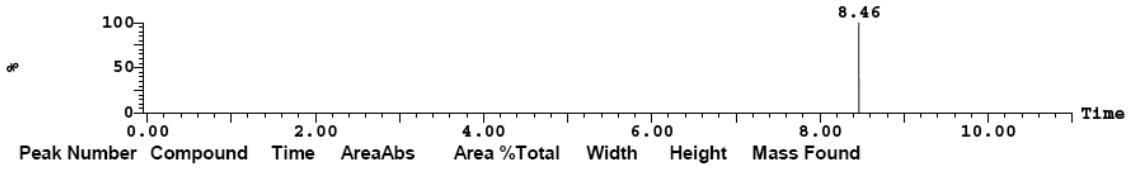


HP-LC-MS Spectrum (SOP 2200) of **4t**. UV purity: 100 %

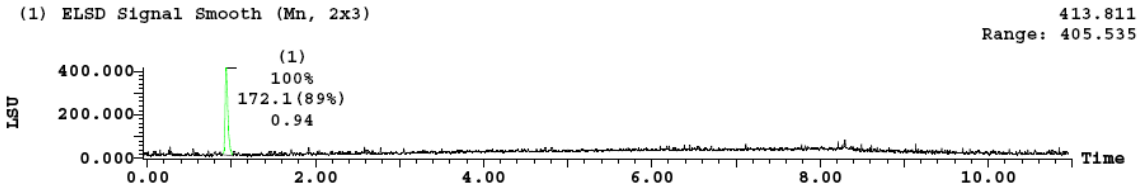




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

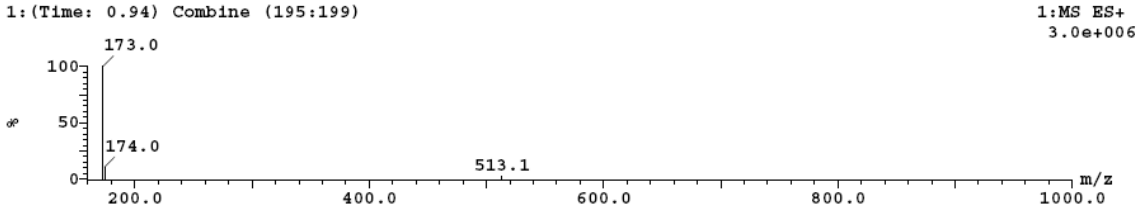


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

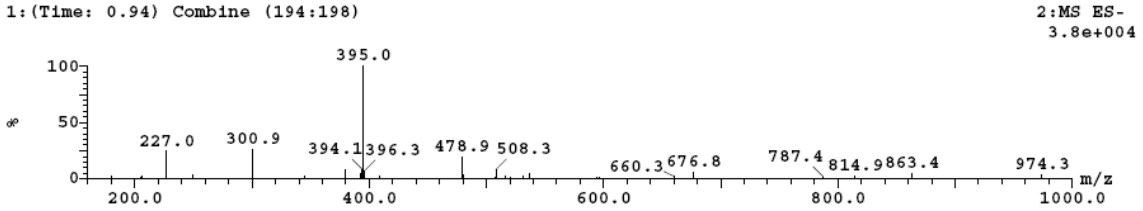


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	0.94	15239.2	100.00	398287.6	172.06

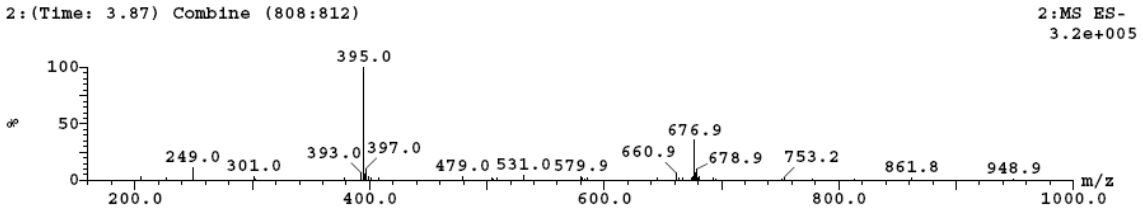
Peak ID	Compound	Time	Mass Found
1	Found	0.94	172.06



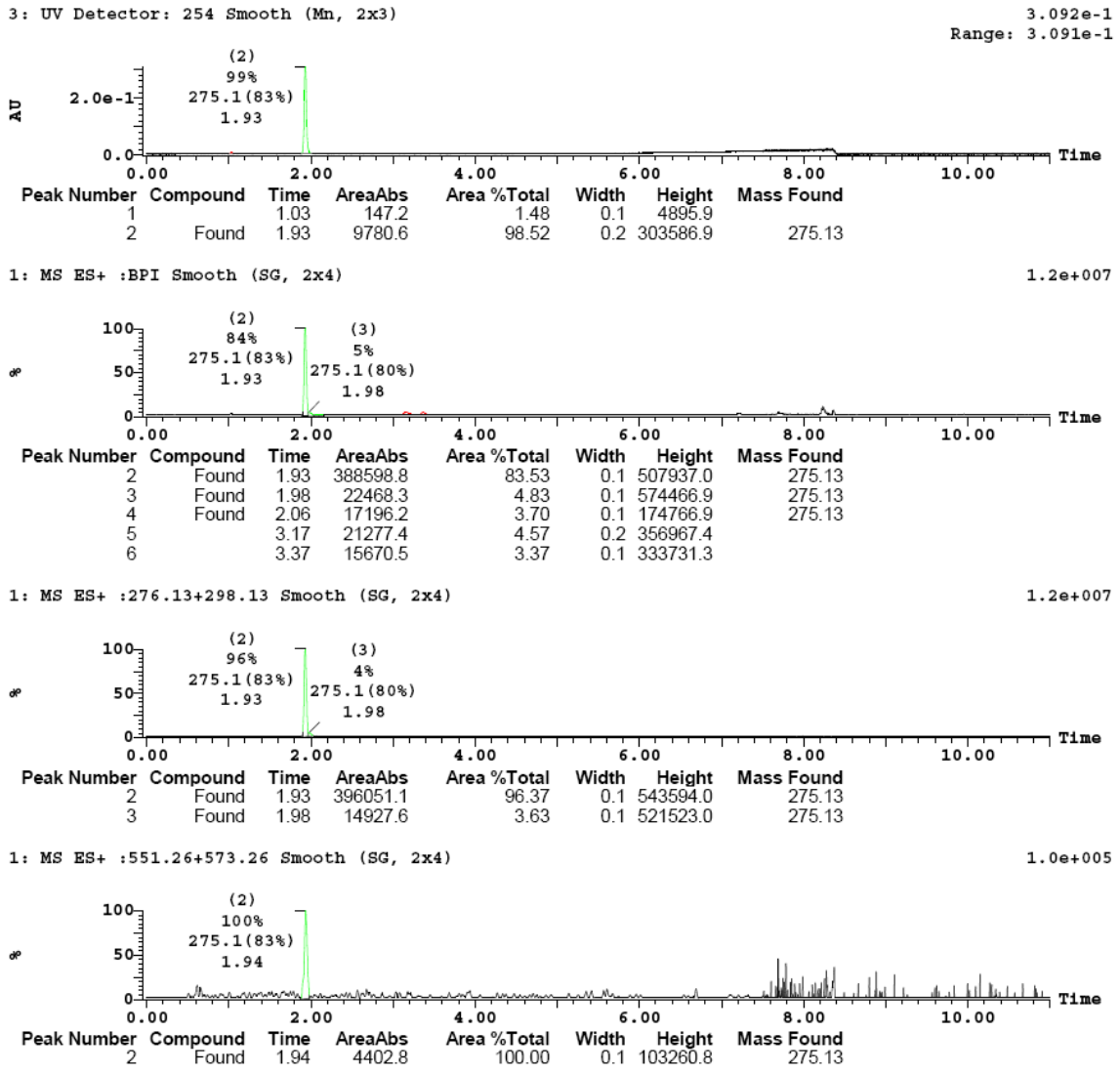
Peak ID	Compound	Time	Mass Found
1		0.94	

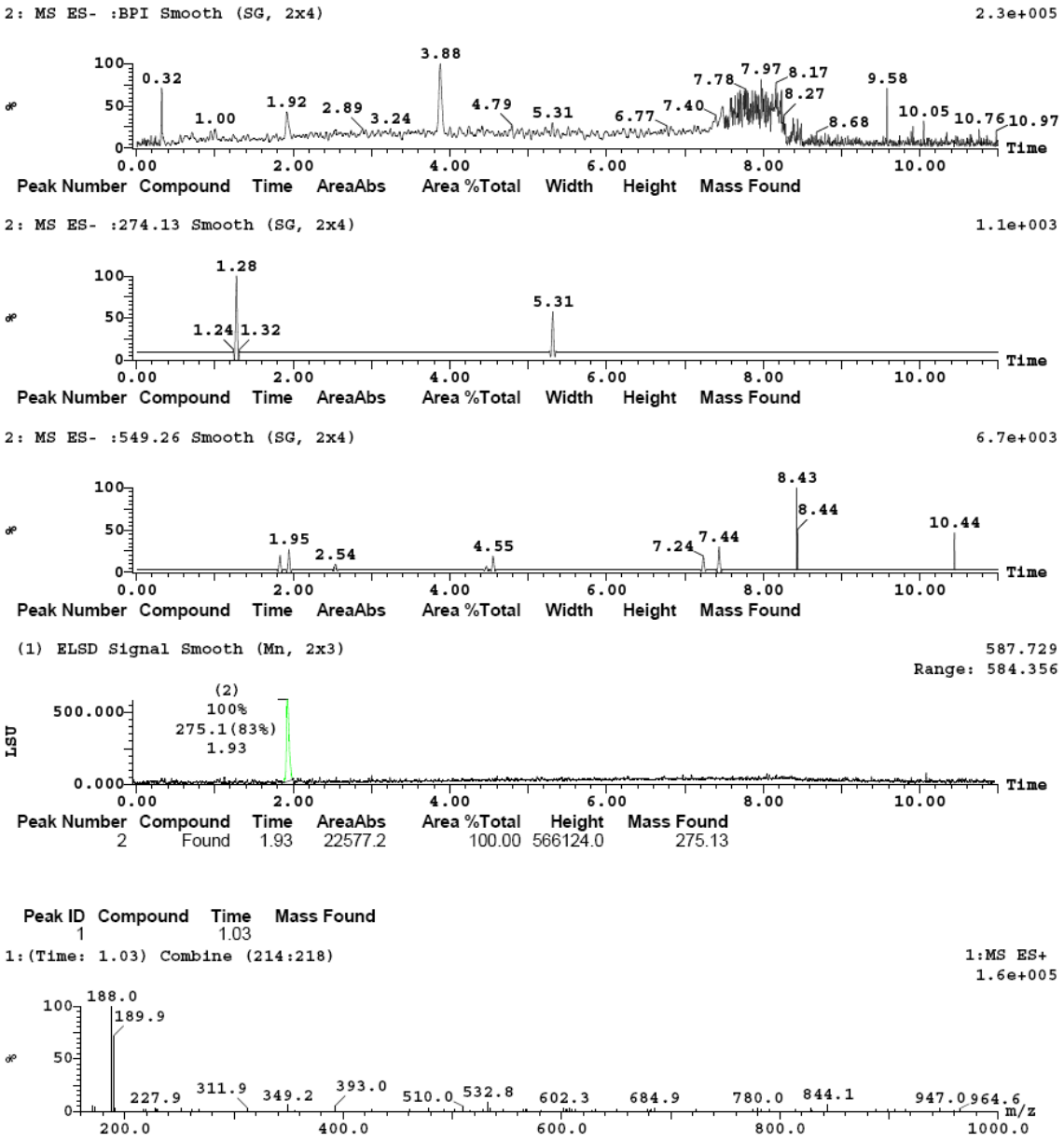


Peak ID	Compound	Time	Mass Found
2		3.87	



HT-LC-MS Spectrum (SOP 2200) of **4u**. UV purity: 98.5 %

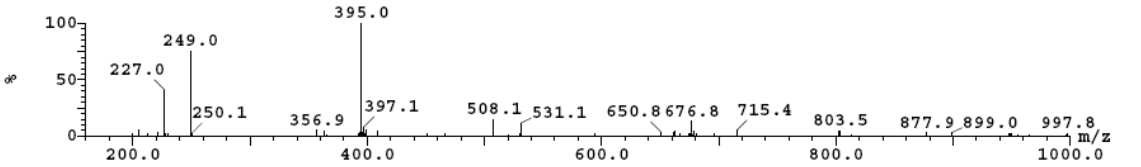



2: MS ES- :BPI Smooth (SG, 2x4)
2.3e+005
0.32
1.00
1.92
2.89
3.24
3.88
4.79
5.31
6.77
7.40
7.78
7.97
8.17
8.27
8.68
9.58
10.05
10.76
10.97
Time
Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found
2: MS ES- :274.13 Smooth (SG, 2x4)
1.1e+003
1.24
1.28
1.32
5.31
Time
Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found
2: MS ES- :549.26 Smooth (SG, 2x4)
6.7e+003
1.95
2.54
4.55
7.24
7.44
8.43
8.44
10.44
Time
Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found
(1) ELSD Signal Smooth (Mn, 2x3)
587.729
Range: 584.356
(2)
100%
275.1(83%)
1.93
500.000
0.000
LSU
Time
Peak Number Compound Time AreaAbs Area %Total Height Mass Found
2 Found 1.93 22577.2 100.00 566124.0 275.13
Peak ID Compound Time Mass Found
1 1.03
1:(Time: 1.03) Combine (214:218)
1:MS ES+
1.6e+005
188.0
189.9
227.9
311.9
349.2
393.0
510.0
532.8
602.3
684.9
780.0
844.1
947.0
964.6
m/z

Peak ID	Compound	Time	Mass Found
1		1.03	

1:(Time: 1.03) Combine (213:218)

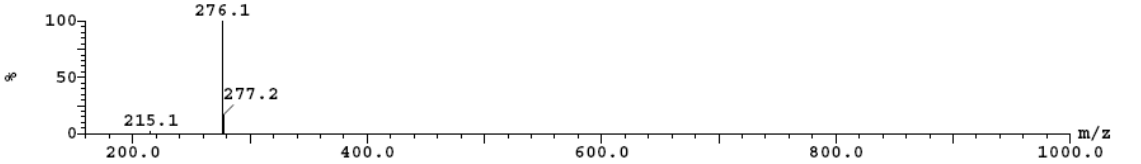
2:MS ES-
2.8e+004



Peak ID	Compound	Time	Mass Found
2	Found	1.93	275.13

2:(Time: 1.93) Combine (401:405)

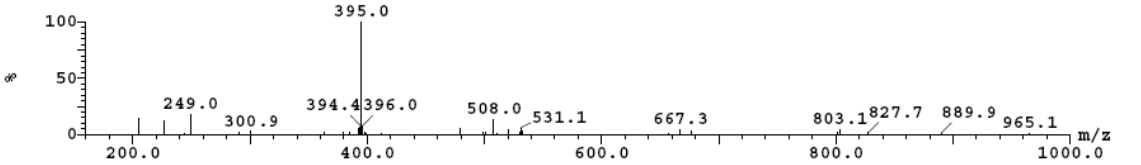
1:MS ES+
1.0e+007



Peak ID	Compound	Time	Mass Found
2		1.93	

2:(Time: 1.93) Combine (401:405)

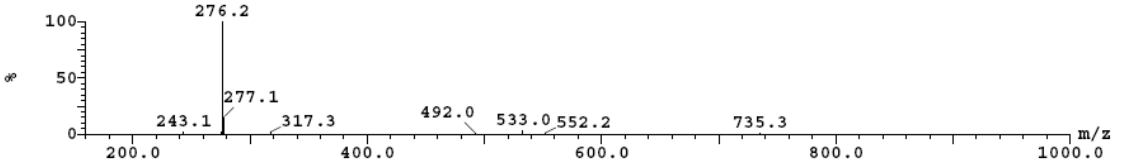
2:MS ES-
1.1e+005



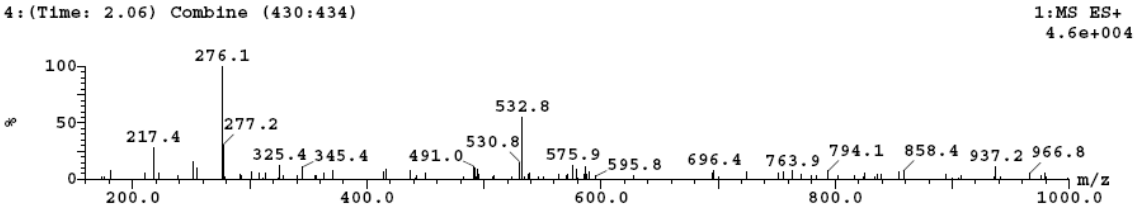
Peak ID	Compound	Time	Mass Found
3	Found	1.98	275.13

3:(Time: 1.98) Combine (412:416)

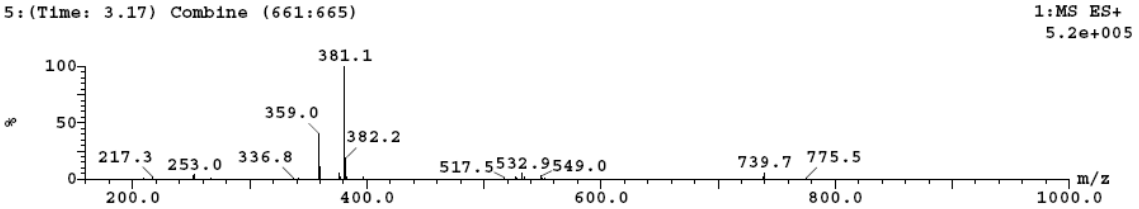
1:MS ES+
5.4e+005



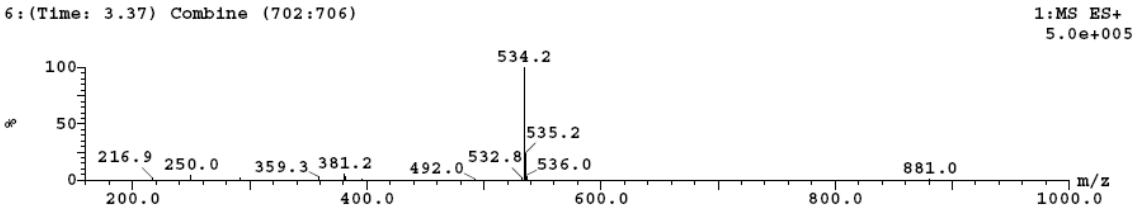
Peak ID	Compound	Time	Mass Found
4	Found	2.06	275.13



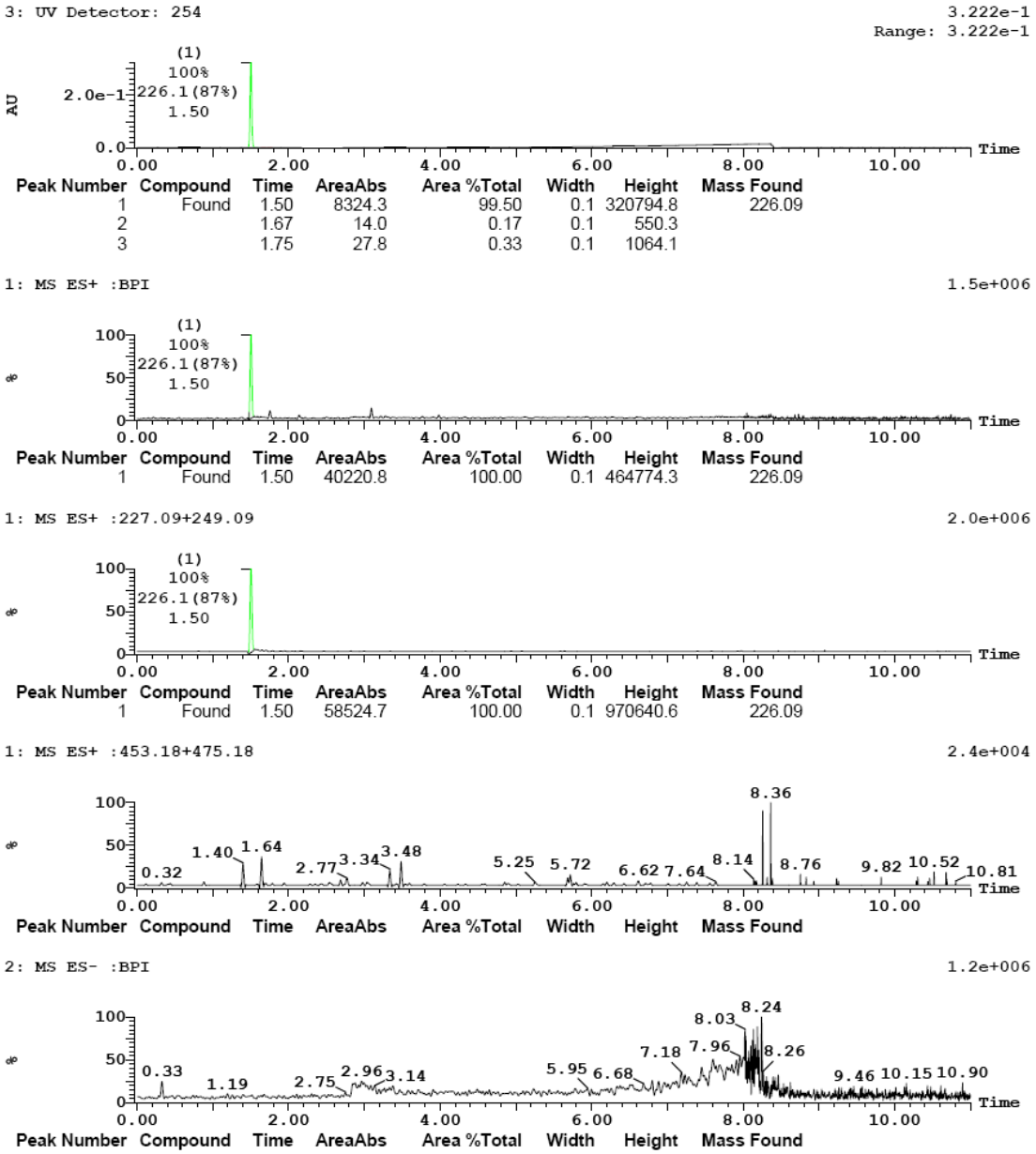
Peak ID	Compound	Time	Mass Found
5		3.17	

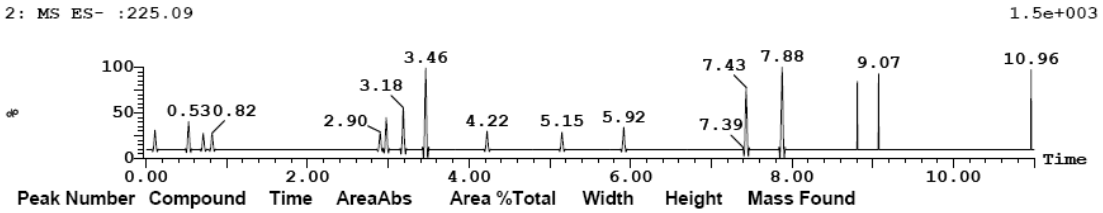


Peak ID	Compound	Time	Mass Found
6		3.37	

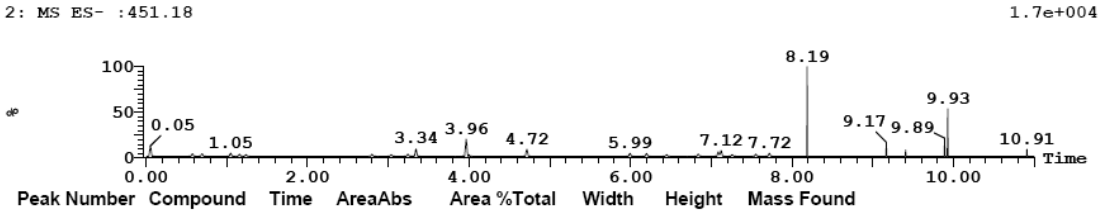


HT-LC-MS Spectrum (SOP 2200) of **5** (*meridianin A*). UV purity: 99.5 %

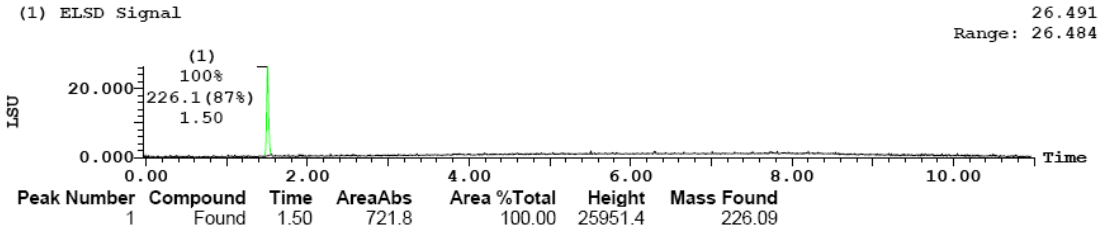




Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

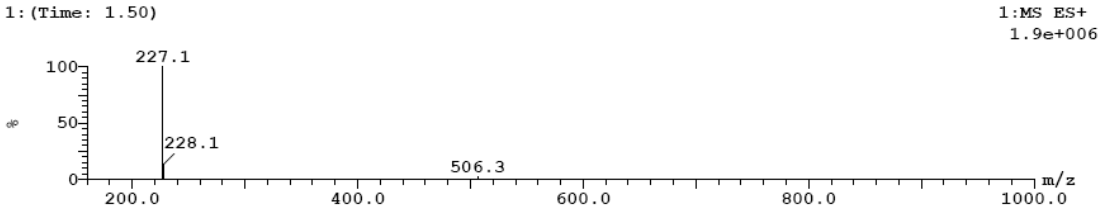


Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found

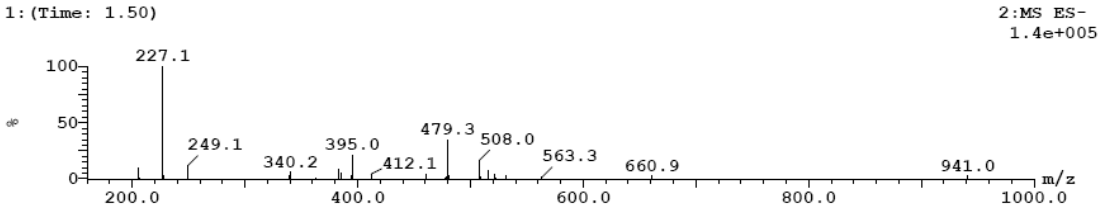


Peak Number	Compound	Time	AreaAbs	Area %Total	Height	Mass Found
1	Found	1.50	721.8	100.00	25951.4	226.09

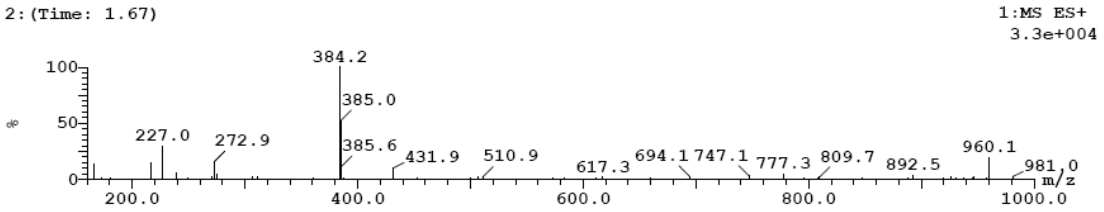
Peak ID	Compound	Time	Mass Found
1	Found	1.50	226.09



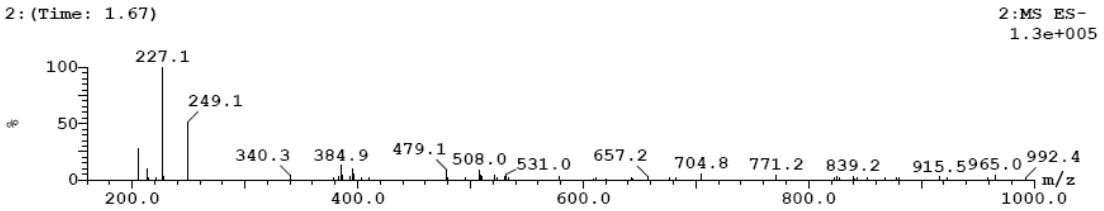
Peak ID	Compound	Time	Mass Found
1		1.50	



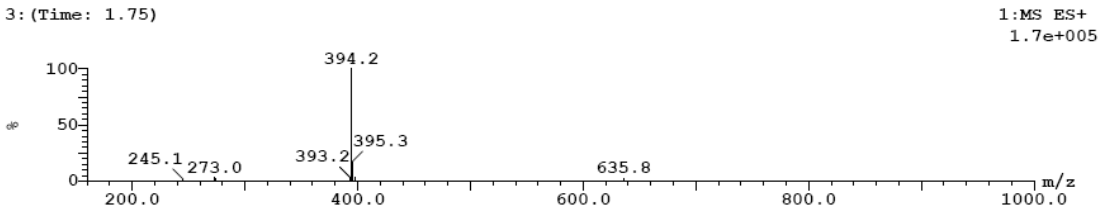
Peak ID	Compound	Time	Mass Found
2		1.67	



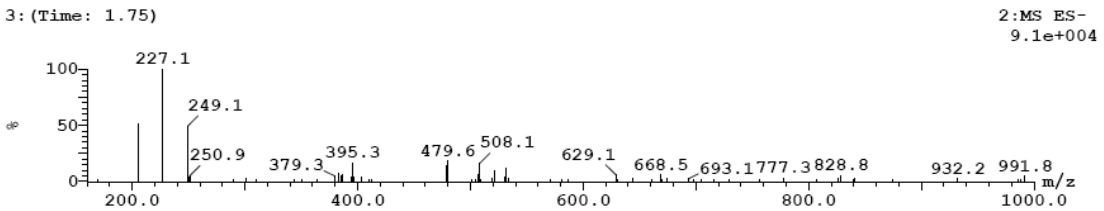
Peak ID	Compound	Time	Mass Found
2		1.67	



Peak ID	Compound	Time	Mass Found
3		1.75	



Peak ID	Compound	Time	Mass Found
3		1.75	



6.2. HT-LC-MS Methods for the Control of Identity and Purity of Compounds 4a-u and 5

Problem Definition	Identity and Purity			
SOP	2200			
Methods	HT-LC-MS			
System	Waters Acquity UPLC® with PDA and ELSD			
	Waters SQD (ESI+/- and APCI+/-)			
Software	MassLynx with OpenLynx			
Column	Waters XBridge™ C8 3.5 µm			
	4.6 x 50 mm Column			
	Part No. 186003053			
Eluent	A: 99.9 % acetonitrile + 0.1 % TFA			
	B: 99.9 % water + 0.1 % TFA			
Gradient	time (min)	A %	B %	flow (mL/min)
	0	5	95	2.0
	8.00	100	0	2.0
	8.10	10	90	2.0
	8.50	5	95	2.0
	11.00	5	95	2.0
Column temperature	Room temperature			
Injection volume	3 µl			
Sample Preparation	Approx. 0.1 mg were dissolved in acetonitrile + water 50/50 in an ultrasonic bath, so that the concentration was 0.5 mM. If necessary, the sample was additionally diluted: 100 µl in 500 µl acetonitrile + water 5/95.			

Problem Definition	Identity and Purity			
SOP	2222			
Methods	HT-LC-MS			
System	4 x Waters 1525 Binary HPLC Pump			
	2 x Waters In-Line Degasser AF			
	1 x Waters 2777 Sample Manager			
	1 x Waters 2488 Mux-UV Detector			
	4 x Waters 2420 ELS Detector			
	1 x Waters ZQ-MUX			
Software	MassLynx with OpenLynx			
Column	Chromolith® Flash RP-18e (25-2mm)			
Eluent	A: 99.9 % acetonitrile + 0.1 % formic acid			
	B: 99.9 % water + 0.1 % formic acid			
Gradient	time (min)	A %	B %	flow (mL/min)
	0	5	95	0.8
	1.7	100	0	0.8
	3.0	100	0	0.8
	3.01	0	100	0.8
	6.25	5	95	0.8
Column temperature	Room temperature			
Throughput	416 samples: approx. 11 hours			

7. References

[1] B. Witulski, N. Buschmann, U. Bergsträßer, *Tetrahedron* **2000**, *56*, 8473-8480.

[2] E. Merkul, C. Boersch, W. Frank, T. J. J. Müller, *Org. Lett.* **2009**, *11*, 2269-2272.

[3] A. S. Karpov, E. Merkul, T. Oeser, T. J. J. Müller, *Chem. Commun.* **2005**, 2581-2583; A. S. Karpov, E. Merkul, T. Oeser, T. J. J. Müller, *Eur. J. Org. Chem.* **2006**, 2991-3000.